A Ciba Foundation Volume

MAN AND HIS FUTURE

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Edited by

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Preface

THE CIBA FOUNDATION arranges many small international conferences, most of them concerned with highly technical, specialized and fundamental aspects of medical research. This book contains the papers and discussions of an exceptional conference. The subject—based on a suggestion first made by Dr. Pincus—could however be looked upon as a reasonable extension of the Foundation's main interests; the aim of all our meetings is to stir the imagination, speed the flow of information, and generally hasten the progress of work in medical and biological research. The world was unprepared socially, politically and ethically for the advent of nuclear power. Now, biological research is in a ferment, creating and promising methods of interference with "natural processes" which could destroy or could transform nearly every aspect of human life which we value.

Urgently, it is necessary for men and women of every race and colour and creed, every intelligent individual of our one world, to consider the present and imminent possibilities. They must be prepared to defend what they hold good for themselves and their neighbours, and, more importantly, to use the immense creative opportunities for a happier and healthier world. This book should make people think.

The occasion for this unusual symposium was the first use of a new conference room at the Foundation's house in Portland Place, London. We are very grateful to the 27 distinguished contributors for their time, effort and imagination—and their co-operation in the preparation of a text which has been modified to some extent in favour of the lay reader. The editor also records his great indebtedness to many others who gave essential and valuable help in the organization of the symposium and the production of this book: Anthony and Marjorie de Reuck, Peggy Cameron, Maeve O'Connor, Julie Knight, Nancy Spufford, John Rivers and William Hill.

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The Future of Man—Evolutionary Aspects

JULIAN HUXLEY

THE evolution of this planet as a unit in the cosmic process has been going on for perhaps 5,000 million years. Life was evolved here after about half of this huge span of time, and has itself been evolving during the later half of the period—to be more precise, for some 2,750 million years. We, like all other living organisms and all other features of the earth, are products of this process of evolution. We men belong to the latest dominant type to be produced, and are now responsible for the future evolution of the planet, which, according to the astronomers and geophysicists, is likely to continue for at least another 2,750 million years.

We are privileged to be living at a crucial moment in the cosmic story, the moment when the vast evolutionary process, in the small person of enquiring man, is becoming conscious of itself.

Evolution can be defined as a natural process of transformation, self-operating and irreversible, which in its course generates novelty, greater variety, more complex organization, and eventually higher levels of mental or psychological activity. And we are discovering that all reality is, in a perfectly legitimate sense, a single and comprehensive process of evolution.

But this comprehensive process falls naturally into three main sectors. The first is the inorganic or cosmic sector, operating by physical or simple chemical interaction, and resulting in the evolution of elements, nebulae, stars and planetary systems; the second is the organic or biological sector, operating by automatic natural selection superposed on physico-chemical interaction, and resulting in the evolution of plant and animal organisms—from fungi and flowers to monkeys and medusae;

the third is the human or psychosocial sector, operating by mind-accompanied psychosocial pressure superposed upon natural selection, and resulting in human societies and their products—from machines and works of art to sciences and religions.

On this earth (and presumably in a few other isolated spots in the universe) there have thus been two critical points in evolution, when it has entered on a new phase, with new properties and characteristics. The first was when, thanks to the evolution of deoxyribonucleic acid (DNA) and genes, material organizations became self-varying and self-reproducing, and the biological phase began to operate. The second was when, thanks to the evolution of conceptual thought, symbolic language and the cumulative transmission of experience by tradition, mental or mind-accompanied organizations became self-varying and self-reproducing, and the human phase emerged.

In the psychosocial phase, the process of evolution is predominantly cultural. Its results are manifested in the variety of societies, and of their organs, like philosophies, legal codes, and social systems.

In this phase a new mechanism for securing continuity and change has been added. In addition to the biological basis of inheritance and variation provided by the gene-complex in the chromosomes, man has a cultural basis, in the shape of the complex of ideas, beliefs and purposes and their transmissible results which is broadly called *tradition*. With its aid, he can accomplish something impossible to any other organism—he can transmit experience cumulatively down the generations and incorporate its results directly into the evolutionary system.

In cultural evolution, there is no sharp distinction between germ-plasm and soma, between genetic basis and its phenotypic results. True, the main stream of tradition is constantly shedding some of its pathological and lunatic fringe, just as the main stream of material germ-plasm is constantly shedding some of its pathological and unhelpful mutants; but in general, culture is simultaneously manifested and transmitted.

The mechanism of biological evolution is now, in broad outline, established. But we are only beginning to study psychosocial evolution in the same operational way. Some things, however, are becoming clear. In the first place, the basic elements in cultural transmission and transformation are psychological: they are patterns and systems of thought and attitude expressed or formulated in transmissible terms, from concepts to values. For want of a better word I shall lump them all together and call them *ideas.* The material elements transmitted—paintings, documents, machines, jewels—are normally vehicles or products of ideas in this loose and general sense.

A more precise term than psychological would be *psychometabolic.* Man is equipped with two metabolisms, two systems for transforming the raw materials of nature in serviceable ways. Physiological metabolism utilizes the raw materials of objective nature and elaborates them into biologically operative physicochemical compounds and systems. Psychometabolism on the other hand utilizes the raw materials of subjective or mind-accompanied experience and elaborates them into psychosocially operative organizations of thought and feeling—including principles like causation, categories like space, abstractions like truth; precepts and concepts, poems and gods, myths and scientific theories, moral commandments and legal codes.

Psychometabolism introduces quality into a quantitative world, produces meaningful patterns out of the chaos of elementary experience, and enables us to grasp extremely complex situations as wholes. Psychometabolic processes may become diseased, as in schizophrenics; their products may be unrelated to the objective world, as with hallucinations; they may be built on false foundations, like racialist ideas; or they may be rendered out of date by the march of knowledge, like the notion of demoniac possession: but they are a necessary part of our psychosocial machinery, and it behoves us to study them thoroughly and understand how they work.

In psychosocial evolution the struggle for existence has been replaced by what might be termed the striving for fulfilment.

The main operative agency in this phase of evolution is psychosocial pressure. This is the resultant of the separate pressures of individuals' loves and hates, desires and hopes, needs and purposes; but it is related to the conflicts and problems thrown up by the march of events, and given direction by some general organization of ideas and beliefs. It has to operate within an organized system of social institutions, which will have arisen out of past ideas and events, but which may often be out of step with later ideas and their results.

As Darwin first pointed out, there has been during biological evolution a general trend towards improvement—improvement in efficiency and in self-regulation. This trend is inevitable, but is accompanied by much waste, suffering, and extinction. The trend towards improvement continues in psychosocial evolution, though again accompanied by suffering, horror and evil. Yet in spite of all the waste and misery, the total improvement achieved during the whole process of evolution, from the origin of life to the present day, is almost incredible—from a submiscroscopic pre-cellular viroid to a self-conscious civilized human vertebrate, throwing up on its way a fantastic profusion of organic and cultural variety.

This is both an encouragement and a challenge. The challenge is man's obvious imperfection as a psychosocial being; both individually and collectively, he is sadly in need of improvement, yet clearly improvable. The encouragement derives from the fact of past improvement. If blind, opportunistic, and automatic natural selection could conjure man out of a viroid in a couple of thousand million years, what could not man's conscious and purposeful efforts achieve even in a couple of million years, let alone in the thousands of millions to which he can reasonably look forward?

The next point to note is that the process of improvement is not continuous. It takes place in steps, by a succession of successful or dominant types of organization, each endowed with new capacities and possibilities. Some once-dominant types become extinct, but many do persist, though in reduced numbers and a subordinate position.

In psychosocial evolution, the dominant types are organizations of thought and belief and of the mind-accompanied behaviour resulting from them: for brevity's sake we may call them idea-systems. Thus in our own history, the early idea-system based on magic and witchcraft became subordinated to the new theological and metaphysical dominant system of medieval Christianity, which in turn has become largely superseded by the scientific idea-system. Today, it looks as if a new dominant idea-system is in process of being born, a system that I will call "evolutionary humanism". Of course, the march of ideas is not an autonomous process, but interlocks with the march of historical events. History presents man with a series of stimuli, often in the form of painful shocks. Human power-lust and cruelty may get out of hand, human stupidity may be unable to take advantage of new opportunities; apparent advance may eventually become frustrating instead of rewarding.

We are now on the threshold of a truly critical step—into the phase of self-conscious evolution. The current phase of human organization is ending in a tangle of unresolved problems and self-defeating activities.

The organization of power in competitive national units has reached its logical conclusion in the confrontation of two great opposed blocs immobilized in the frozen grip of the cold war. Advance in the technical efficiency of weaponry has given us weapons so powerful that they cannot—we hope—be used: meanwhile the nations are spending so much on armaments that there is not enough to meet more than a fraction of other and more important psychosocial needs.

Increasing emphasis on material products has led to wasteful over-exploitation of nature and a threatened shortage of natural resources. The technical efficiency of agricultural and industrial production is producing surpluses which cannot be disposed of and is beginning to throw people out of work, and yet is unable to meet the essential requirements of the needy throughout the world. Medical science has become so spectacularly efficient that population is exploding and outrunning resources. Excessive preoccupation with quantity of material

goods has led to neglect of quality in life. In general, man's exploration and control of external nature has far outrun his exploration and control of his own nature.

However, there is one field in which real and decisive advance is being made—the field of knowledge and understanding. Here, for the first time, man is being given a reasonably comprehensive and reasonably correct vision of himself, of his own nature, and of his place in nature—in other words, his destiny: a broad picture of the unitary evolutionary process and of what his rôle in it might be.

There have been many situations in biological evolution where a successful type of organization has apparently realized all the main possibilities open to it. Further advance can then only be achieved through the rise of a new type with a new pattern of organization and new possibilities of development. Today, the passage to a new phase is being made possible by this new picture of human destiny. In place of the conflicting aims of the present, our new vision is already indicating the single and over-riding aim of fulfilment—greater fulfilment for more individuals and fuller achievement by more societies, through greater realization of human possibilities and fuller enjoyment of human capacities.

This new vision inevitably results from our new knowledge, though only with the aid of intellectual and imaginative effort. It could and should provide the basis for an operational system of ideas and beliefs to support and guide us in the next phase of our psychosocial evolution. Thus we must make every effort to clarify this new vision of destiny, to follow out its implications, and set it to work. An obvious first task is to examine the outstanding problem situations of the present, in the light of this dawning idea-system.

There is first the increasing psychosocial pressure caused by the convergence of the psychosocial process upon itself. This, as Teilhard de Chardin pointed out in *The Phenomenon of Man*[1], is due to the apparently banal fact that man's habitat is the surface of a globe. During his brief history, he has multiplied his numbers and improved his communications, until his

societies have spread over the whole habitable area of the earth, and are impinging on each other politically, economically, and ideologically.

The world has become a unit *de facto:* sooner rather than later, it must become a unit *de jure*, by submitting itself to a unitary system of self-government. Since the human habitat is one and indivisible, its resources must be explored as a global whole. And since thought knows no frontiers, ideas of every kind are diffusing faster and faster all over the world's surface, demanding recognition, posing questions, generating conflicts.

The units of organization which have proved most effective during biological evolution are bounded unit-systems of great internal complexity, whose components are engaged in a constant and vigorous interplay, leading to their mutual reinforcement within an integrated total pattern of activity. Such self-bounded and complex systems include the cell, the vertebrate individual, the social insect colony, and the brains of higher mammals and man. When such a system ensures the constant circuiting, summation, and interaction of nervous impulses, as does the human brain, it generates a high level of subjective experience.

Thus, since the advent of man, a new habitat has been opened up to evolving life, a habitat of thought: for this I shall use Teilhard de Chardin's term, the nöosphere, until someone invents something better. This covering of the earth's sphericity with a thinking envelope, whose components are interacting with a steadily rising intensity, is now generating a powerful psychosocial pressure favouring a solution of least effort, by way of integration in a unitary organization of ideas and beliefs. But this will not happen automatically: it can only be achieved by a large-scale co-operative exercise of human reason and imagination.

When we look at the whole sweep of man's history on earth, as now revealed by the labours of historians, archaeologists, and anthropologists, we see that everything that properly deserves to be called progress has depended on new knowledge and new organizations of knowledge in the shape of ideas. Agriculture,

monotheism, mathematics, marine navigation, the scientific method, the industrial revolution, the conquest of infectious disease and the prolongation of life—all have depended upon the growth of knowledge and its better organization.

We have discovered that each advance may lead us into difficulties, but also that evolution is a dialectic or cybernetic process operating by feedback, in which new difficulties can be surmounted, but only with the aid of new discoveries and new applications of knowledge.

During the past three centuries the most powerful agency for providing new knowledge has been Science. I use the word, spelt thus with a capital letter, in the continental sense to include all branches of organized rational enquiry, including the natural sciences, the social and psychological sciences, and the various humanistic sciences, such as history and philosophy, aesthetics and comparative religion; and as opposed to all speculative and *a priori* philosophies and untested explanatory systems.

Today, science too is being bent in on itself by the earth's sphericity. Its spectacular advance since the Renaissance has been achieved by successive invasions of separate fields of enquiry—mechanics, astronomy, physics and chemistry, natural history and geology, physiology and biology, anthropology, psychology and sociology. This type of separate and sometimes competitive scientific expansion is now reaching its limit. There are still some vacant areas to explore, like space research or extrasensory perception; but science as a whole cannot escape the pressure towards integration.

In place of separate subjects each with their own assumptions, methodology and technical jargon, we must envisage networks of co-operative investigation, with common methods and terminology, all eventually linked up in a comprehensive process of enquiry. This, of course, will mean a radical reorganization of scientific teaching and research.

If man is responsible for the future of this planet, he must pay more attention to ecology—the science of relations between organisms and the resources of their environment.

Human ecology involves finding out what resources are available in our environment and how to make the best use of them. We have to think first of all of material resources—minerals, water-power, soil, forests, agricultural production—but we must also think of the non-material or enjoyment resources of the habitat, such as natural beauty and solitude, interest and adventure, wild scenery and wild life.

The two types of resource are interlinked. Thus in eastern Africa, the assemblage of splendid large mammals and birds, the last remnant of the climax community of prehuman evolution, is one of the world's unique enjoyment resources. But it is of immediate financial value, through tourism, to the local inhabitants. It is also of physiological value: large areas of the dry savannah lands of the region degenerate if cultivated or used for grazing cattle. But if they are properly managed, their communities of wild animals yield large amounts of "wild protein" for human food—larger than can be obtained from domestic stock.

During much of man's evolution he has been busily engaged in ruining his own habitat. We have been doing so in Britain, for instance, by polluting our rivers. The Thames was once a fine salmon river, and Henry II is said to have fed the polar bear given to him by the King of Norway by letting it out from the Tower of London at the end of a rope to fish for itself. The river was also famed for its oysters. Today, almost its only abundant animal is the little red worm *Tubifex*, which specializes on survival in dirty oxygen-poor mud. Detergents and heated cooling water as well as sewage and general filth are ruining one river after another.

A new ecological threat of man against his own habitat has recently appeared, in the shape of pesticidal chemicals, both insecticides and herbicides. As Rachel Carson has brought out with devastating clarity in her book[2] *The Silent Spring*, these are now destroying the ecological pattern of the countryside. Apple and clover crops are failing because their pollinators, the bees, are being wiped out. Pesticides are depauperating the plant-rich verges of our country roads, and killing off lovely and

harmless flowers as well as so-called weeds. By killing caterpillars, they have caused the virtual disappearance of many of our butterflies and have sadly reduced the population of cuckoos and various songbirds. Numbers of birds are killed directly by eating poisoned grain, and others rendered sterile by the poisoned flesh of the insects and other creatures they eat. Enjoyment as well as material resources are being threatened; as my brother Aldous said after reading Rachel Carson's book, we are exterminating half the basis of English poetry!

Scientific ecology gives the basis for good land use. I have already pointed out how important a proper land-use policy is in underdeveloped countries like Africa. It is equally important, though for rather other reasons, in overcrowded and highly developed countries like our own. In Britain, for instance, we have an actual shortage of space, and there is constant pressure on the land's surface for a variety of different and even conflicting forms of use—for house-building, for communication, for industry, for military purposes, and for enjoyment. Somehow different forms of land use must be amicably co-ordinated, so that one form of use is paramount in one area, another in another. Proper land-use planning is applied human ecology.

Biologically-minded planners must also think about long-term ecological changes affecting the human habitat. Thus it appears probable that the present interglacial and relatively mild climate will continue for well over 5,000 years, with consequent melting of ice-caps, raising of the absolute sea-level, and threatened flooding of large areas of coastal flatlands (except in the arctic and subarctic, where isostatic recovery will continue to raise the land and lower the relative sea-level for about 4,000 years); but that, on the basis of Milankovich's and van Woerkom's calculations, this will be succeeded, a little over 10,000 years from now, by the onset of a new cold period of increasing glaciation.

Man lives in three kinds of habitat, the planetary, the social and the psychological. The planetary habitat, the concern of ecology in the ordinary sense, I have just been discussing. To

deal with the problems of the social habitat, which man has created himself, we need a science of social ecology.

The outstanding social habitat is the city, the habitat of civilized man; as Lewis Mumford has so beautifully demonstrated in his great book[3], *The City in History*, the history of cities is also the history of civilization. However, cities are now becoming self-defeating; if the growth of human civilization is to be fostered and not frustrated, it will be necessary to devote more and more attention to the social ecology of cities. Thus mere increase of size and numbers beyond a certain point brings its own problems of traffic congestion, commuting, and general frustration, and bad planning in the past necessitates so-called urban renewal in the present.

The city also can provide important enjoyment resources, not only as a centre for entertainment and the arts, but also in visual enjoyment of good planning and fine architecture.

Next we come to psychological ecology—the mind's investigation of itself and its own psychological habitat. We must explore qualitative inner space as well as quantitative outer space. This, of course, includes the exploration of our own individual minds and their operations, and also exploration of the nöosphere, the realm of thought and feeling which our minds create in interaction with the fact of experience, the psychological habitat in which we live and on whose resources we must draw.

As regards our individual minds, the main aim must be to canalize their development so as to reconcile or transcend conflicting drives and impulses, and to develop effective psychological bonds with other individuals and with nature around us. Much of this will be psychotechnology.

This will help us to correct various unfortunate tendencies—the tendency to find scapegoats for one's own guilt, the tendency to put off one's own responsibilities on to someone or something else, as when we ascribe our own wishes and purposes to the State or to God. It will help to prevent us discharging our aggressive impulses and our hates in wrong and dangerous ways, and help us to avoid reification—erecting abstractions to

the status of real entities, thinking that there is any such *thing* as "truth" or "virtue".

We need co-ordinated research on all methods of attaining states of self-transcendent experience: on yoga, both physical and psychological; on directed meditation; on hypnotism in all its extraordinary manifestations; on dreams and their possible control; on apparent "possession" by an alien personality or spirit, as in medicine-men or shamans, or as in Haitian voodoo; on ecstatic or trance-like experiences produced by dancing, as in many tribal societies. In many cases, joint participation enhances and socializes the effect; this is so in voodoo, in tribal dances, and in the confraternities of dancing dervishes.

Meanwhile, physiology and biochemistry are indicating new areas for us to explore. For instance, it has now been shown that in man as well as in animals, electric stimulation of a particular area in the brain can produce an overwhelming sense of happiness or well-being in the whole organism. It has even been found possible to make one half of the body feel happy, while the other half remains in its normal state. To some people this seems somehow too materialistic; but after all, electric happiness is still happiness, and happiness is very much more important than the physical happenings with which it is correlated.

Perhaps even more exciting possibilities are being opened up by drugs, like mescalin, lysergic acid, and psilocybin, which can produce astonishing results in minute doses. They are called "psychedelics" because they reveal new capacities of the human psyche. They appear to do this by modifying the psychometabolic machinery which builds up our perceptual world. In schizophrenia, some chemical substance, itself possibly due to a genetic error of metabolism, is apparently interfering with this process, so as to produce disorderly perception. Psychedelic drugs, on the other hand, seem to release the process from the need to check its results against outer experience. No longer forced to achieve coherence with the outer world of sense, it can produce inner experiences of great intensity and variety,

with a coherence of their own. With some people in some circumstances, the experiences can be horribly distressing, but with others, perhaps the majority, they can be intensely releasing and satisfying.

The ritualization of shared transcendent experience to serve as a communal bond is a frequent feature of so-called primitive societies, as in the mescalin-induced but essentially religious peyote ceremonies of some North American Indians. We need to discover how it could be utilized in our more elaborate civilized communities. My brother Aldous has made some suggestions about this in his practical Utopia, *Island*[4].

Then there is the problem of economics. Our present economic system is rapidly becoming self-defeating. It is all geared to the supposed need for growth—a steady increase of production. The Western economic system, which is steadily invading new regions, is turning into what has been called *consumerism*. As one American writer has put it, the Western economy depends on persuading more people to believe that they want to consume more products. This is leading to over-exploitation of resources which ought to be conserved; to excessive concentration on advertising of saleable products; to the neglect of recipes for healthy and happy living (compare the large amounts still spent on advertising cigarettes with the small amount devoted to advertising their harmful effects in promoting lung cancer); and to the dissipation of talent and energy into non-productive channels. In the Soviet Union, on the other hand, we have what may be called *productionism*, partly to satisfy the obvious consumer needs of the population, but largely to keep up with and eventually to outstrip the United States in industrial efficiency.

The system leads to local over-production combined with world maldistribution. It is now being threatened by its own over-efficiency, first in respect of mass-production and now of automation. This is leading to underemployment (which is already serious in countries like India, and will shortly become serious in the United States and Britain) and to more compul-

sory leisure. Even if it were decided to stop the armaments race, nobody seems to know how to adjust our economy to such a drastic change.

I am not an economist: I would only suggest that we start looking at the problem from the other end, and aim at a world-wide system based on the idea that progressively fewer man-hours will be needed to furnish the material substructure of life, but progressively more man-hours for occupying the time that is freed, a system in which the stigma of not being employed full-time would be removed. In other words, we need a fulfilment economy, aimed at providing opportunity for everyone to find some interesting or significant occupation during the half or more of their time which will not be gainfully employed in production.

This will be as radical a change as that from a barter to a money economy, or from a regulated system of production and trade to *laisser faire* capitalism: but what an exciting opportunity for the economists and sociologists!

Another urgent field for evolving man to explore is that of his own population increase. This is posing the most serious problems for his future, not merely in the long term but also in the short term of two or three generations only. The situation, in brief, is this. In the past half-century there has been an unprecedented population explosion, the result of so-called death control. Modern medicine and health measures have been so successful that they have drastically reduced mortality and much increased the expectation of life (though not the total life span). The human population only reached the thousand million mark early in this century; it is today just about 3,000 million; and whatever measures we undertake now, will more than double itself by the year 2000, within the life-time of many of us alive today. Not only has the absolute number of human beings been increasing, but also their rate of increase. The compound interest rate of world population-increase cannot have exceeded one-tenth of one per cent per annum for many millennia. It reached one per cent only in the present century. Today it is more than 1·8 per cent, and is still apparently going

up. Several countries have even achieved the unenviable record of 3 per cent, which means doubling in 23 years.

As a result, the world's population is beginning to press harder and harder on the world's resources. Even now, perhaps half the total number of people in the world are inadequately nourished; in developed countries like Britain or Holland there is pressure on mere space; in under-developed countries, more and more marginal land is being cultivated, more and more forests are being cut down, more and more soil is being eroded.

What are we to do about it? Some people have suggested that we should export our surplus to other planets: they can never have thought quantitatively about the problem. This would mean shipping off a hundred human beings every minute. One thing is certain: the process cannot go on unchecked for more than two or three generations at most without leading to disastrous trouble. Thus, it is impossible to industrialize under-developed and already densely populated countries if too much of the capital and skill needed for the process are swallowed up in feeding, housing and looking after too many children. A country like India must cut its birth-rate in half within half a century if it is to achieve successful industrial development: it is salutary to realize that, even if it did so, its population would still be increasing faster than Europe's in its nineteenth-century heyday.

Over-multiplication may also lead to aggressive imperialist expansion. This happened in pre-war Germany, with its claim for *Lebensraum;* it happened with pre-war Japan; and it rather looks as if it is happening now in post-war China.

The fall-out from the population explosion is already affecting us in many unpleasant ways. Over-increase of population leads inevitably to over-large cities; and this, as we see for ourselves in our daily London lives, leads to traffic paralysis, to frustrating rush and long hours of commuting for millions of men and women, and to the city-dweller being more and more completely cut off from nature. More and more elaborate bureaucratic regulation becomes necessary, and might all too easily lead on to some form of authoritarianism.

The problem also has important psychological aspects. In rats and other mammals, excessive crowding seriously distorts behaviour: there is much fighting, and the normal processes of reproduction are interfered with. There can be little doubt that some comparable neuroendocrine disturbance occurs when human beings are overcrowded: there is increasing frustration and irritation and the resultant tension can readily lead to outbreaks of violence and other anti-social behaviour.

The world needs a population policy. We must stop thinking in terms of a race between the production of food and the production of people; we must begin thinking in terms of a balance between people and the various resources they need. To achieve this, we must balance death-control with some form of birth-control, with the immediate aim of reducing the rate of population-increase and the ultimate aim of achieving a balanced adjustment instead of an unbalanced maladjustment.

To do this we must first of all overcome a great deal of moral, ideological and religious resistance. This can only be done by helping people understand that to oppose proper methods of birth control is radically immoral since it condemns an increasing number of human beings to increasing misery, frustration and ill-health.

Meanwhile, all advanced nations should devote an increasing amount of scientific and technological manpower to discovering and perfecting simple and acceptable methods of birth-control, and making their discoveries freely available to the rest of the world. For another thing, international aid should take account of what I may call the demographic credit-worthiness of the recipient. If the aid is likely to go down the drain of excess population, the recipient country should be encouraged and helped to initiate an efficient policy of population-control, and some of the aid should be devoted to seeing that the policy is effective.

We must also make the world at large aware that the whole future of mankind is endangered: if present trends continue unchecked man will become the cancer of the planet instead of the guide and director of its further evolution.

The population explosion is making us ask the fundamental question—so fundamental that it is usually not asked at all—what are people for? Whatever the answer, whether to achieve greater efficiency or power, or, as I am suggesting, to find greater fulfilment, it is clear that the general quality of the world's population is not very high, is beginning to deteriorate, and should and could be improved. It is deteriorating, thanks to genetic defectives who would otherwise have died being kept alive, and thanks to the crop of new mutations due to fall-out. In modern man the direction of genetic evolution has started to change its sign, from positive to negative, from advance to retreat: we must manage to put it back on its age-old course of positive improvement.

The improvement of human genetic quality by eugenic methods would take a great load of suffering and frustration off the shoulders of evolving humanity, and would much increase both enjoyment and efficiency. Let me give one example. The general level of genetic intelligence could theoretically be raised by eugenic selection; and even a slight rise in its average level would give a marked increase in the number of the outstandingly intelligent and capable people needed to run our increasingly complex societies. Thus a 1·5 per cent increase in mean genetic intelligence quotient (I.Q.), from 100 to 101·5, would increase the production of those with an I.Q. of 160 and over by about 50 per cent.

How to implement a eugenic policy in practice is another matter. The effects of merely encouraging potentially well-endowed individuals to have more children, and *vice versa*, would be much too slow for modern psychosocial evolution. Eugenics will eventually have to have recourse to methods like multiple artificial insemination by preferred donors of high genetic quality, as Professor Muller emphasized a quarter of a century ago, and I re-emphasized in my recent Galton Lecture. Such a policy will not be easy to execute. However, I confidently look forward to a time when eugenic improvement will become one of the major aims of mankind.

Education is another subject of basic concern for human evolution, for it transmits and can transform the tradition in and by which we live. There are many disputes about education, but no dispute that it needs radical improvement if it is to do its job successfully in man's rapidly changing life.

In the first place, education must aim to give an overall picture of the world we have to live in and of ourselves who have to live in it, instead of dishing up a curriculum in a series of separate "subjects". It can sketch in the broad outlines of such a picture at a very early age, provided that a general approach is used from the outset; and it is quite possible to give a coherent picture and some real understanding by the age of 15 or 16, provided that no attempt is made to present children with a premature doctrinal synthesis and that the curriculum is properly planned so that subjects (or as I would prefer to say, fields of study) are not overburdened with details, do not compete, but reinforce each other in a total pattern.

In such an integrated curriculum, the evolutionary-historical idea could provide a central core and the ecological idea could cover the branching interrelation of subjects, while the idea of science, art, religion and literature as psychosocial organs would bring the sciences and the humanities into partnership. Such a curriculum would go a long way, not only towards bridging the gap between C. P. Snow's two cultures, but also towards making the process of learning much more interesting and enjoyable. I remember Bertrand Russell once exclaiming "Isn't it nice to know things!": our educational system ought to ensure that the average boy and girl can echo this sentiment.

Of course education must also equip people with specialized knowledge and specialized skills, but we must beware both of excessive and of premature specialization.

In addition to a curriculum of subjects, we need something quite new—a properly thought-out curriculum of experience: discovery through projects and travel, through group studies and adventure, through participation in activities felt to be worth while. In such ways, education could provide for greater fulfilment as well as for better learning.

In particular, education in the next phase should pay a great deal of attention to non-verbal education of all sorts. It should help children to explore the possibilities of their own bodies, of perception, of imagination, of creative activity, of the enjoyment of beauty and art. Though art in the broad sense is one of the major functions of man, the arts are lamentably neglected in our educational system, especially in its higher reaches.

Man is the most variable of all organisms, and the new education must take full account of this basic fact. Human variety is a source of strength to society, and we must encourage it and not try to impose uniformity. The educational system should take Roger Williams' dictum *Free but Unequal* as its motto, and make *Varied Excellence* its aim.

At the moment we are encouraging verbalizers and discouraging visualizers, and also encouraging quick and docile learning and discouraging imagination and creativity. We need an Education Council to initiate research into this and every other aspect of the educational process.

One fundamental aim of education should be to help children to develop an integrated personality. For this to be successful, the educational profession will have to take full account of modern psychology and psychiatry, and to do a great deal of research on the best methods of enabling children to by-pass or transcend conflict and to arrive at a better integration of their inner selves.

Education should also help to transform cultural tradition. It can do this if the basic idea-system which it puts before growing minds is an evolutionary one, in which the ideas of possible improvement and the vast extent of unrealized possibility are implicitly and explicitly stressed. If it provides boys and girls with opportunities of fulfilment during their school career, this will make them protagonists of a real fulfilment society in the future. In such ways, education could become an efficient agency of further human evolution.

I would have liked to say something about the situation in other organs of evolving man—about art as simultaneously creating and interpreting complexity and variety in ways

impossible to logic or discursive exposition; about religion as a psychosocial organ relating man in some significant way with the powers and forces that move him from within and batter on him from without, an agency for expressing, affirming, and struggling with his destiny in mingled awe and adoration. But I have neither the competence or the space.

Let me summarize my theme. First, we biologists have to think of the future of man in the unfamiliar terms of psychosocial or cultural evolution.

Looking back, we see that evolving man has lurched from one crisis to another. Great empires have collapsed, whole civilizations have been violently destroyed; thought has been muzzled, common people cruelly exploited, habitats ruined. One dominant phase of psychosocial evolution after another has reached a limit and has had to crumble and be remodelled or replaced if human advance was to continue. Yet in the long term there has been advance, and new advance has always sprung from new ideas, new knowledge and its applications.

The present phase of the process is rapidly becoming self-limiting and self-defeating. If we fail to control our economic system, we over-exploit our resources. If we fail to prevent atomic war, we destroy civilization. If we fail to control our population, we destroy our habitat and our culture. However, our increasing knowledge is indicating how we might remodel our psychosocial organization and escape from the apparent impasse.

The new and central factor in the present situation is that the evolutionary process, in the person of mankind, has for the first time become conscious of itself. We are realizing that we need a global evolutionary policy, to which we shall have to adjust our economic and social and national policies.

To succeed in this we need to reorganize our science—to switch the various branches of science out of their separate channels, and bring them together in a co-operative effort. In particular, we must switch more and more of our scientific efforts from the exploration of outer space to that of inner

space—the realm of our own minds, and the psychometabolic processes at work in it. It is here that the greatest discoveries will be made, here that the largest and most fruitful territories await our occupancy. All branches of science and learning, from biophysics to social anthropology, from psychiatry to aesthetics, can join in this great venture of exploration.

We should set about planning a Fulfilment Society, rather than a Welfare Society or an Efficiency Society or a Power Society. Greater fulfilment can only come about by the realization of more of our potentialities. Once people grasp what a small fraction of humanity's potentialities are actually being realized, and what vast new possibilities are waiting to be elicited, we shall have a new and powerful motive to activate our future.

Our knowledge of the evolutionary past makes it clear that any new psychosocial system should be open-ended, not liable to become self-limiting. Like science itself, human evolution must become a self-correcting cybernetic process.

Our present civilization is becoming dysgenic. To reverse this grave trend, we must use our genetical knowledge to the full, and develop new techniques of human reproduction, such as oral contraception and multiple insemination by deep-frozen sperm from desired donors. Eventually, the prospect of radical eugenic improvement could become one of the mainsprings of man's evolutionary advance.

Meanwhile, since evolutionary advance depends on knowledge, we must try to secure the widest possible dissemination of modern knowledge and ideas about our evolutionary rôle and the possibilities of fulfilment, must raise the level of education in all sections of all nations, and must remodel our educational systems so that they can promote transformation as well as transmit tradition.

To me, it is an exciting fact that man, after he appeared to have been dethroned from his supremacy, demoted from his central position in the universe to the status of an insignificant inhabitant of a small outlying planet of one among millions of stars, has now become reinstated in a key position, one of the

rare spearheads or torchbearers, or trustees—choose your metaphor according to taste!—of advance in the cosmic process of evolution.

The present is a challenging moment, when for the first time we can see ourselves in the long perspective of that extraordinary process, can get a better view of its operation and direction, and can bring all our resources of knowledge and will to bear on the dual task of avoiding immediate disaster and realizing new possibilities in the long future. In this dual task, only scientific method and a massive deployment of scientific manpower can prevent disaster and ensure evolutionary improvement.

Agricultural Productivity in relation to Population

COLIN CLARK

"A LIFETIME of malnutrition and actual hunger is the lot of at least two thirds of mankind." This extraordinary misstatement, which is in fact based on an arithmetical error, is believed by almost everyone, because they have heard it so often. It was first made in 1950 by Lord Boyd Orr[1], who had just retired from the post of Director General of FAO (Food and Agriculture Organization of the United Nations). A search for the evidence on which this statement is supposed to have been based was undertaken by M. K. Bennett[2], Director of the Food Research Institute at Stanford University and a recognized world authority in this field.

The text of FAO's *Second World Food Survey*, which was not published until 1952, but which appears to have contained the material on which Lord Boyd Orr was working, included a statistical table for which neither sources nor methods of compilation were given. This table purported to show average calorie requirements per head of all the nations in the world, and compared these with supposed data of calorie supplies—data which, for most of the countries in question, have not since been republished, because of serious doubts about their accuracy.

"One cannot escape the inference", Bennett writes, that Boyd Orr had completely misunderstood the nature of the statistics (inaccurate in any case) which had been placed before him; and had taken as supposed minimum requirements, below which people would actually suffer hunger, a set of figures of "targets" for production at some time in the future, which targets FAO itself had already abandoned.

FAO was once sardonically described by *The Economist* (23 August 1952) as "a permanent institution devoted to proving

that there is not enough food in the world". There is unfortunately a considerable element of truth in this accusation; though it is also true, as *The Economist* went on to say, that FAO "gives much useful practical advice and assistance" regarding food production and distribution throughout the world.

One of the most valuable tasks which FAO has undertaken has been to organize the preparation, by a group of the leading physiologists in this field, of thorough and agreed studies of what are, in fact, people's food requirements, measured in calories, under varying circumstances; the first of these[3] was published in 1950, and an improved and enlarged version[4] in 1957. This report provides the basis for the calculations given below.

A similar attempt by FAO (1957) to obtain a report on the quantity and composition of man's protein requirements was inconclusive[5]. However, a community even at the lowest levels of agricultural productivity, living predominantly on cereals, even coarse cereals such as barley, maize, sorghum or millet, if they have enough calories, will also receive enough protein, though this is not the case with peoples living predominantly on root crops such as cassava, sweet potatoes, yams and taro.

There is no doubt that shortages of vitamins and minerals in the diet may have serious effects upon health, and may sometimes be fatal. It is generally agreed, however, that such shortages are not very likely to arise in a primitive nomadic or peasant community whose food, though scanty, is nevertheless obtained directly from natural sources.

In May 1961, Dr. Sukhatme, FAO's own Director of Statistics, in a paper to the Royal Statistical Society in London[6], made a skilful mathematical analysis of the limited information available on the distribution of food consumption and concluded that the proportion of the world's population which was hungry was 10 to 15 per cent. Discussion by an expert audience confirmed this conclusion, subject to the possibility that the extent of hunger in China might be rather greater, and in the rest of Asia rather less, than Dr. Sukhatme had stated.

But is it not the case, many people may ask, that it is possible to have a diet adequate in calories, or "starchy foods", but still to suffer serious malnutrition through lack of adequate quantities of the "protective foods"? When I was working with Lord Boyd Orr in the 1930's this was clearly understood[7]. We required 100 grams of fat per head per day, 68 grams of protein, at least half of which had to be obtained from animal sources, 0·9 grams of calcium, which had to be obtained from dairy products and vegetables and not by enriching flour; and so on. Subsequent advances in physiological science have caused all these figures to be abandoned. Some recent work by Brock and Waterlow has indicated that true protein needs may be much less than was previously supposed (3 grams per kilogram body-weight per day for infants, falling progressively to 0·5 gram for adults) and that very little of the protein need be of animal origin.

An attempt to state baldly the average calorie requirements of any population, as is often done, may lead to serious error. Requirements of calories are functionally related, though not directly proportional to the weight of the body. Less food is required to maintain body temperature in a warm climate than in a cold one. Active physical work increases calorie requirements, as also do pregnancy and lactation.

The calculations which follow are based on Table 7, p.45, in the 1957 FAO report on calorie requirements[4] which relates to such a population, with both birth and death rates fairly high, and a high proportion of children and of pregnant and lactating women in the population.

The objection sometimes raised, that these varying body weights themselves are the consequence of varying levels of nutrition, is best met by Table I. Between castes which have been living, probably for many generations, at violently contrasted levels of nutrition, the differences in body-weight are slight.

Calorie requirements obtained[8] from direct measurements of calorie requirements (computed per hour from the rate of oxygen consumption as measured by the Douglas bag) of

Table I

FOOD CONSUMPTION AND BODY-WEIGHTS OF DIFFERENT CASTES IN AN INDIAN VILLAGE

	Average income (Rupees/person/ month)	*Food consumption (calories/ person/day)*	*Average body-weights of adults (kg.) Male*	*Female*
Fishermen	6·5	1580	48	41
Harijans (low caste)	7·5	1940	46	40
Miscellaneous castes	10	1960	48	41
Agricultural castes	8	2440	49	42
Brahmins and Vaisyas	18	2720	51	45

Africans in Nigeria working at various tasks are used as the basis of Table II. Two alternative sets of calculations are made: for men averaging four hours' field work a day, approximately the present situation in Africa, and for men doing eight hours' work a day, a rate of work which prevails in China and the Caribbean and which may prevail in Africa in the future. The apportionment of time for the rest of the day is admittedly highly conjectural.

For field work, Phillips's figures[9], adjusted by Trowell[10], range from 213 calories per hour for carrying a log of 20 kilograms, to 269 for grass cutting, 274 for hoeing, the principal agricultural activity of Africans, 360 for sawing, 372 for bush clearing, and 504 for tree felling. It is well known, however, that men engaged in extremely arduous tasks such as the latter cannot work continuously. The FAO calorie report (1957) quotes (p. 59) an estimate by Lehmann to the effect that men engaged in such work, if they are to preserve their health, must be allowed rest pauses, which bring their average for calorie consumption down to 300 per hour. Converting to African body weight, and reducing slightly, we take a figure of 250 calories per hour for working consumption.

The average body weight, however, had to be fairly arbitrarily assumed. The average temperatures also were only approximately estimated from an examination of maps of isotherms.

We must now re-express these calories, with concomitant

Table II

CALORIE REQUIREMENTS OF A "YOUNG" POPULATION WITH HIGH BIRTH AND DEATH RATES

	Assumed body weights of adults (kg.)		*Tempera-ture (C°)*	*Calories/day required by men aged 20–29*							*Calorie requirements/day/head of total population*					
	Men	*Women*									*Component varying with temperature only: Children under 15*	*Components varying with temperature and body-weight: Women*	*Men*		*TOTAL*	
FAO estimates	50	40	25				2445				727	447	779		1953	
FAO estimates for African weight	57·5	—	25				2707									
Hours/day field work done by men					4			8					4	8	4	8
					hr./day	Cal./hr.	Cal./day	hr./day	Cal./hr.	Cal./day						
				Field work	4	250	1000	8	250	2000						
				Other active work and re-creation (e.g. housebuilding, dancing)	1	250	250	1	250	250						
				Walking	2	184	368	1	184	184						
				Sedentary activities	9	78	702	6	78	468						
				Sleeping	8	62·5	500	8	62·5	500						
Central Africa	57·5	50	25				2820			3402	727	526	897	1084	2150	2337
India, SE Asia	50	40	25				2545			3070	727	447	811	978	1985	2152
S China	50	40	20				2614			3153	747	459	834	1003	2040	2209
N China	55	45	10				2735			3300	786	528	871	1051	2185	2365

protein, in the form of quantities of cereals required. One kilogram of wheat or similar grain, which in the hands even of the poorest cultivator must be milled down to 900 grams, will then yield 3,150 calories. It follows that a community living entirely on grain, with a few wild plants or pills or other source to supply vitamins and minerals, will require, at the rates of daily requirements shown in the table, anything from 630 to 750 grams per person per day, or 230–274 kilograms per person per year. These figures might be reduced by about 5 per cent for people consuming certain millets, which have higher caloric values than other grains.

The protein content of grain is very variable, but it averages over eleven per cent. People consuming grain at this rate, therefore, would obtain sufficient protein.

Studies by FAO (1960) show that even the poorest communities require about 1·5 kilograms per person per year of textile fibres[11], representing about 10 kilograms of grain, if we base our equivalent on the quantity of agricultural resources needed to produce it. Allowing for this, and also for the grain equivalent of small quantities of animal protein, green vegetables, etc., required, we can estimate subsistence as 250–300 kilograms of grain equivalent per person per year. We can define this as a "subsistence unit".

It must be added that the diets to which we have become accustomed in North America, Western Europe and Australasia represent about ten times subsistence requirements. This does not, of course, mean that we eat more cereal; in fact we eat much less. The rest is made up of the meat, milk, eggs, bacon, fruit, etc., which have required large quantities of cereals to be fed to livestock in order that they might be produced, or have used up the grain equivalent of substantial quantities of agricultural land and labour. Many doctors tell us that we would be healthier if we ate less.

We will consider the agricultural resources, both labour and land, required to produce one unit of subsistence, that is to say, the amount of agricultural production which would provide a necessary minimum of food and clothing for one person for a

year; we can multiply for whatever factor we think fit, up to our own factor of ten, if we wish to provide a more agreeable and palatable diet. The Japanese, for example, are quite a healthy and prosperous people on the world scale, who only consume a little over two subsistence units each. They are content with a diet of rice, vegetables and a small quantity of fish, not very different from that of their ancestors.

The number of subsistence units which can be produced by one man's labour may vary from 1,000 produced by one man, aided by suppliers of equipment, fertilizers, transport, etc., on the Canadian prairies, to the poorest African cultivator, who can only produce subsistence for four or five working the whole year through.

The amount of land required to provide for one person varies of course according to whether we are living at one or ten times subsistence level, but it also varies enormously according to our methods of food production.

Before we begin to specify areas, we must take into account man's need of wood, as well as of food and fibres. Our descendants, with all the nuclear power they want at their command, should not need fuel wood. Other requirements may range from 2 cubic metres round wood per person per year in the United States and Canada to not much more than 0·5 cubic metre in western European countries, which have to import wood. We do not really need more, even for houses. As timber prices have gone up, and concrete technology has improved, considerable economies in the use of wood have been effected; FAO have reported (1957) that the quantity of wood[12] used in an average western European house fell from 9·1 to 7·6 cubic metres in the short period 1950–55. The North American wastes forest products in the excessive size of his newspapers and other advertising and in the abundance and thickness of his wrappings. It would be better to impose a heavy tax on wood pulp, to conserve forests, to make the collecting of waste paper worth while, and to reduce litter.

Wood consumption at the rate of 0·5 cubic metre can be restated at about 250 kilograms dry matter per person per year,

or a similar order of magnitude to our *minimum* food requirements.

In any case, the plants which we grow for food produce only a certain proportion of their substance in the form of starches, sugars, proteins, etc., which we can eat. The rest, apart from water content, consists of fibres which we plough back into the soil, or feed to animals, though occasionally we can use them for textiles or pulp.

The palaeolithic hunter required 10 square kilometres per person to feed himself; the neolithic herdsman, 0·1 square kilometre, or 10 hectares; the medieval peasant two thirds of a hectare of ploughland to produce cereals for subsistence, plus his woodland: the Indian rice grower one fifth of a hectare to produce subsistence; the Japanese one sixteenth of a hectare, or only 640 square metres. It is the growth of population, as we shall see below, which has provoked these agricultural improvements. But we are still far from the end of the road.

Let us take a look into the distant future, at our descendants possibly living in much larger numbers on this earth, or even living in communities with carefully conserved supplies of oxygen and water, on inhospitable planets, or on natural or artificial satellites. If our descendants reach the numbers which are sometimes predicted for them, they are likely, in the process, also to attain levels of wealth and technical skill which would make such tasks as building artificial satellites and transferring colonies of people to them quite feasible. They would not, presumably, have to engage in hard physical labour. If we take the basic allowance of 250 kilograms for food and double it, to allow for some wood and wood pulp, and to provide a little variety for the diet, we have a requirement of 500 kilograms per person per year or 1,370 grams per person per day. We can also assume those improvements in chemistry which would enable them to use the whole dry weight of the plant, either as food or as fibre. How much space would be required to produce this amount of plant material, dry weight, under the best conditions? In others words, what are the best rates of photosynthesis in grams per square metre per day, which have been

observed in nature, or in agricultural laboratories?

Algae have received a lot of attention—they have the incidental advantage that they can use up sewage—but they rarely have a yield of more than 20 grams dry matter per square metre per day. In July, the warmest—and often the wettest—month of the year in England, potatoes and sugarbeet grow at a rate of 30 grams of dry matter per square metre per day or more. In the tropics, rates of 50, so long as heat and water are available, have been shown by sugar cane, elephant grass, and water hyacinth. The latter is a most troublesome weed which grows in waterways, but Pirie has very sensibly suggested that it should be grazed by hippopotamus, manatee or other marine animals, which yield good meat. Experiments in the agricultural laboratory at Oxford have shown that, under carefully controlled conditions, the familiar radish and broccoli can grow at 40 to 45 grams of dry matter per square metre per day. In open air in England the corn cockle has been found to grow at 57—which is why the farmers find it such a dangerous weed.

If we settle for 50 grams per square metre per day, then the growth of each person's requirements of food and fibre requires only 27 square metres. This is the sort of information which may be required in the future by the designers of space ships and artificial satellites. Even this figure may be reduced further, as we come to learn more about the exceptionally complex and tricky process of photosynthesis. The theoretical maximum rate of photosynthesis has been calculated at seven times our figure of 50 grams per square metre per day.

Malthus thought that human populations always tended to increase up to the limits of available subsistence, after which their growth was checked by "vice and misery". Historical, geographical and anthropological evidence—most of which, to be fair, was not available to Malthus—alike show how untrue his proposition was. Primitive hunting and fishing peoples, who are able to make virtually no provision for the sick and infirm, suffer such high mortality that even reproduction at the maximum rate biologically possible only just maintains their numbers. When eventually the population rose so that adequate

land was no longer available to provide subsistence in the manner hitherto customary, our ancestors had to turn, no doubt with great reluctance, to domesticating animals and to agriculture.

Even after the establishment of agriculture, historical records show that periods of sustained population growth are rare, and stagnation or decline frequent.

The real success story of population growth provoking economic improvement, the model for other countries to follow, is Japan. When the modernization of the country began, Japan was a poorer and more backward country than any Asian country is now. Population was growing at the rate of 1 per cent per annum, soon to rise to a rate of nearly 2 per cent. Unlike African and many Asian countries, which have considerable land to spare, Japan was already, in the nineteenth century, very densely populated. Nevertheless, from the 1880's onwards, the Japanese were able to increase the output from their own agriculture and fisheries, quite apart from any food they could import, at the rate of 3·5 per cent per annum, far ahead of the rate of population increase. This rate of improvement in agricultural production was continued up to the 1920's, by which time Japan had little need to worry, as she was earning enough from exports to import a considerable part of her food requirements, as Britain does.

Let us not, however, talk as if we were trying to force the whole of mankind on to a cereal diet. Even if it is not physiologically necessary, we enjoy a diet of meat and dairy products. How much land is required to produce them, if we do the job properly?

Let us take as our standard the United States rate of consumption of meat, 90 kilograms per person per year, half of which is to be in the form of beef and mutton produced from grass, and half pig and poultry meat from cereals. To produce 1 kilogram of pigmeat (corresponding to 1·33 kilograms of live pig) requires, in the hands of good pig breeders, 5·3 kilograms of cereals. To produce 1 kilogram of poultry meat (1·5 kilograms of live bird) requires, in the best modern practice, 3·75

kilograms of feed, equivalent to about 4 kilograms of cereals, if we take into account the agricultural value of protein and other supplements included in the feed. On these figures, therefore, we could provide 45 kilograms of meat from the cereals grown on 580 square metres.

To produce 45 kilograms in the form of mutton and beef would require 20,000 square metres (5 acres) on the "rough grazings" of this country. This land is about as productive as if we did not farm it at all, but merely trapped the rabbits, deer and other wild animals it carried. Farmers improve pasture land by fertilizing, weed destruction, reseeding and controlled grazing. There are many good farmers in Britain who would produce this amount of meat on 2,000 square metres (0·5 acre). The Grassland Research Station has a number of examples of carefully managed grasslands in this country where the figure has been reduced to 1,000 square metres, that is, 1 ton of meat liveweight, or a little over half a ton of meat deadweight per hectare per year. With good management it is believed that a ton of meat, live weight, should be obtainable from the consumption of 7 tons of grass (dry weight measure). The best fertilized grasslands at the Hannah Institute in Scotland (likewise grass in New Zealand) have yielded 15 tons dry weight per hectare per year, which should be capable of giving double the above meat yield. At this rate we could obtain 45 kilograms of mutton and beef from only 400 square metres.

Americans now consume milk at the rate of 285 kilograms per person per year, including the milk equivalent of dairy products; but their doctors have been telling them that they consume too much, particularly in middle age, when they heighten the risk of coronary trouble; we may take 250 kilograms per person per year as an objective. The average British or North American cow yields 3 tons and, fed entirely on grass, hay and silage, needs 5·5 tons dry weight per year. To allow for the cost of breeding replacement stock, and with a small credit for the meat from old cattle, we may raise this figure to 7·5 tons, or the produce of 5,000 square metres under the best conditions. One person's milk requirements (at 250 kilograms

per year, or one-twelfth of a cow's yield) thus could also be produced on a little over 400 square metres.

Grassland in the high rainfall tropics is shown to be capable, when fertilized, of producing three times as much as the best temperate grassland. Such land is also capable of producing three cereal or leguminous crops per year, if properly fertilized. There have even been cases of fertilized tropical grasslands producing at the rate of 80 tons dry weight per hectare per year, or more than five times the maximum temperate climate yield. Our land requirements, therefore, using the best agricultural methods now available—though great further improvements will be possible—in a temperate climate, not for a subsistence diet, but for our accustomed rich diet, may be expressed as follows:

	Square metres/person
Cereals, sugar, etc.	500
45 kg. pig and poultry meat	500
45 kg. beef and mutton	400
250 kg. milk	400
	1800 or 5·5 persons/hectare

Excluding the wet tropics, defined as lands with a hot climate and rain available for most or all of the year, the world has the equivalent of 6,660 million hectares of good agricultural land[13]. This does not include land which has to be made productive by irrigation, but only the land naturally capable of agriculture, including, in some parts of the world, poor soils requiring considerable fertilization. Where the land is dry for a substantial part of the year, as in much of India, or has excessively long winters, as in northern Sweden, a proportion of its productive capacity is discounted in compiling this total; thus, a hectare of the coldest farm lands in Scandinavia has been entered as only half a hectare; a hectare of grazing land in Australia as only one-thirtieth of a hectare.

The wet tropics contain 510 million hectares of potential agricultural land—158 million each in Africa and Latin America, the remainder in southeast Asia—equivalent to

1,530 million hectares of temperate land. We must have 8,200 million hectares in all, capable of giving a diet containing meat and dairy products on a North American scale to 45,000 million people.

Finally, let me mention our requirements of minerals. They are being reduced by technical improvements and our descendants will not have to worry about mineral fuels, since they will have all the energy they want in the form of nuclear power, solar batteries, and cars driven by batteries or hydrogen, if necessary. The only exception is aluminium, but we could produce this from ordinary clays if supplies of bauxite ran out. If we assume a world population of 45,000 million consuming minerals at the present North American rate per head, the supplies of these minerals available in the top 1,500 metres of the earth's crust would keep them going for some multiple of 10^5 years (10^8 in the case of aluminium).

So it looks like being a long time before our descendants have to dig deeper into the earth—or search in other planets outside it—for minerals.

Sophisticated Diets and Man's Health

J. F. BROCK

For 99 per cent of the time that man has been on earth he was a food gatherer—a root-grubber, berry-picker, locust-eater, beach-comber, fisherman, hunter—and only during the remaining 1 per cent has he been a food producer—herdsman, farmer, dairyman. TIBOR MENDE.

SOPHISTICATION OF FOODS

BEFORE I can begin to discuss the effects of sophisticated diets, it is necessary to define the meanings I have given to these terms in this context.

I have adopted the definition of the Oxford English Dictionary: sophisticated = "altered from or deprived of primitive simplicity or naturalness". The term might reasonably be applied to the diets consumed by those holding privileged positions of leadership and authority ever since man adopted a social organization in advance of the rural group or clan.

One can use the term "sophisticated" in its application to food in several senses:

Firstly, the selective breeding and feeding of vegetables and animals to the point where they contain a balance of nutrients markedly different from original wild types. This is exemplified by selective breeding of cereals and roots so that they contain a very high proportion of carbohydrate in relation to other nutrients and particularly to protein. It is also exemplified by the breeding and fattening of animals so that their flesh and products such as milk contain an excess of fat in relation to other nutrients, particularly protein.

Secondly, the selection of special parts of vegetables or animal foods for consumption by privileged people because of their special appeal through flavour, odour or supposed

special nutritive value. When this selection is made by privileged groups the remainder of the vegetable or animal is usually consumed by the less privileged. This is exemplified by the ancient privilege of a meal of nightingales' tongues, and in modern times by the refining of cereal flours and by the separation of cream from milk.

Thirdly, the culinary art—this may well have begun before the discovery of fire, but the latter established a pattern of sophistication through cooking. It was followed by the titillation of taste through the addition of spices and condiments. Fourthly, these ancient forms of food sophistication have been followed, particularly in the twentieth century, by a remarkable development in industrial food technology. This has involved processing, preserving, colouring and otherwise treating foods so that they are available to the consumer in parts of the world far removed from the source of their production and in forms which extend greatly the three ancient variations of sophistication already mentioned. These technological processes may add a wide variety of preservatives, colouring agents and contaminants to natural foods. Also in the twentieth century agriculturalists and veterinarians have applied to growing plants and animals growth stimulants, pesticides and other devices for accelerating or raising yields. These result increasingly in the presence of contaminants in vegetable and animal foodstuffs in both their fresh and preserved forms. I refer to oestrogens, antibiotics and a variety of substances represented by inorganic arsenic and parathion.

The first three forms of sophistication have been going on for thousands of years but have affected a very small minority of each community or population. The fourth group has popularized the processes of sophistication in such a way that sophisticated foods are consumed by a large proportion of the population in developed or privileged nations. I propose, therefore, to concentrate particularly on the fourth or twentieth century forms of sophistication.

HEALTH

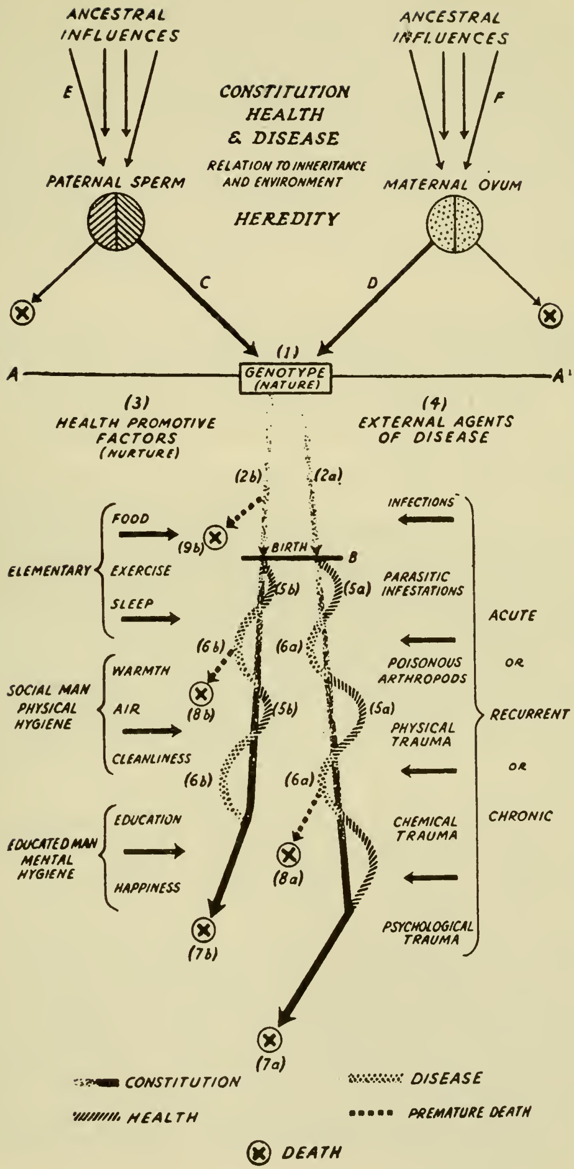
Against a necessary background of health as an all-embracing "wholeness" which is relevant to every section of this symposium it is my task to concentrate particularly on "physical or bodily health". This can be either promoted by favourable environment or impaired by unfavourable environment (Fig. 1). For each individual there is a fixed genotype which is the raw material upon which environment operates and which determines in considerable part the pattern of both health and disease. This genotype is determined by the pattern of chromosome and gene inheritance from father and mother.

The state of health or disease on any one day is favourably or unfavourably determined in part by recent environment, such as a good holiday or exposure to infection. It is determined, however, also by the long-term product of environment and genotype. Thus, the reaction of the body to recent exposure to the tubercle bacillus may be determined, in part, by the favourable effect of rest, good food, physical exercise and recreation during a recent holiday. But it will be determined also by the long-term product of genotype and healthy or unhealthy upbringing, including the mixture of immunity and sensitivity induced by previous exposure to the tubercle bacillus. This long-term product I prefer to call, in the case of physical health and disease, "physical constitution".

I am well aware that another use of the term "constitution" has been advocated by Bauer[1] in the sense of "the sum total of an individual's characteristics as they are potentially determined at the moment of fertilization", but I reject this usage. That, to me, is the genotype. The physical constitution as preferably defined[2] is of great importance in determining man's

Fig. 1. Diagram illustrating relationships between genotype and environment, both favourable and unfavourable, in determining the development of constitution and life expectation, and of experience of health and disease. The long-term progressive development of a healthy and of an unhealthy constitution are shown in the vertical straight lines; the short-term experiences of health and disease are shown in the sinuous deflections about the straight lines.

(From Brock, J. F. (1961), *Recent Advances in Human Nutrition*. London: Churchill.)


ANCESTRAL INFLUENCES
E
CONSTITUTION
HEALTH
& DISEASE
RELATION TO INHERITANCE AND ENVIRONMENT
HEREDITY
ANCESTRAL INFLUENCES
F
PATERNAL SPERM
MATERNAL OVUM
C
D
(1)
A
GENOTYPE (NATURE)
A'
(3)
HEALTH PROMOTIVE FACTORS (NURTURE)
(4)
EXTERNAL AGENTS OF DISEASE
(2b)
(2a)
ELEMENTARY
FOOD
EXERCISE
SLEEP
(9b)
BIRTH
B
(5b)
(5a)
(6b)
(6a)
(8b)
SOCIAL MAN PHYSICAL HYGIENE
WARMTH
AIR
CLEANLINESS
(6b)
(6a)
(8a)
EDUCATED MAN MENTAL HYGIENE
EDUCATION
HAPPINESS
(7b)
(7a)
INFECTIONS
PARASITIC INFESTATIONS
POISONOUS ARTHROPODS
PHYSICAL TRAUMA
CHEMICAL TRAUMA
PSYCHOLOGICAL TRAUMA
ACUTE
OR
RECURRENT
OR
CHRONIC
CONSTITUTION
HEALTH
DISEASE
PREMATURE DEATH
DEATH

experience of health and his resistance to most forms of disease. The concept can be extended to cover many other aspects of man's "wholeness". We can talk about his intellectual, his psychic, and his emotional constitution. All are long-term products of inheritance and environment. All are of great relevance to many aspects of this symposium. I shall, however, be confining my consideration largely to "physical constitution". In a later section I shall be tracing the important effects of habitual dietary pattern on physical constitution.

DIETS

Dietetic restrictions and taboos are very evident in the Bible and other ancient writings, including those of pre-Hippocratic Greece. Some of these had relevance to the hygiene of their day, and still have relevance in some twentieth century under-developed communities.

The beginnings of a naturalistic approach to the subject are seen in two of the Hippocratic treatises—*A Regimen for Health* and *Tradition in Medicine*. Subsequently, considerable attention was given to diet as a factor in health promotion by the ancient physicians. Galen dealt with dietetic aspects of longevity, a theme which is repeatedly encountered in Byzantine and medieval Arabic writings. During the Renaissance, following Luigi Cornaro's *Discourses on a Temperate Life*, the doctrine of dietary discretion as a means of prolonging life became well-established.

The profession of dietetics has developed in the twentieth century out of the science of human nutrition. Therapeutic dietetics has remained within medical control, the dietitian merely constructing and supplying certain diets on principles laid down by practising doctors. Health-promotive dietetics has become the province of a multiplicity of nutrition authorities in consultation with the medical profession and has been developed on an international scale by the World Health and Food and Agriculture Organizations of the United Nations.

Both therapeutic and preventive dietetics have, under the influence of twentieth-century science, become sophisticated in the sense defined.

THE EFFECT OF TWENTIETH-CENTURY SOPHISTICATION OF FOOD AND DIETS ON CONSTITUTION

In the light of the foregoing definitions, I propose to discuss, in relation to the trends evident in the twentieth century, the advantages conferred by all forms of sophistication of food and diets, the evident disadvantages to health, and the possible disadvantages to health in the light both of scientific probability and of food faddism.

ADVANTAGES OF SOPHISTICATION

The advantages of sophistication can best be considered in two parts: firstly the non-physical, which include intellectual, emotional and spiritual advantages; and secondly the physical.

Culinary Art and Culture

The non-physical advantages are evident right back to the earliest stages of sophistication.

Eating should be a social grace as well as a physical necessity. In terms of my definition of constitution the social value of eating is very relevant to man's constitution and therefore to his biological future. I emphasize the word "social" because good food and good wine are not for the friendless man—they are essentially aids to closer contact of mind and spirit between man and man (including women). All of the first three forms of sophistication have served this purpose down the ages. Like all good things they can be abused. One abuse, namely the selfish monopoly of good food by the privileged few, can now be more easily corrected through the greater availability of good food which has resulted from the food technology of the twentieth century.

The culinary art which grew out of the ancient forms of food sophistication has also, when discreetly used, inspired man through the ages, to art, music, philosophy and spirituality in the broadest sense. Again, this claim is not nullified by the evident fact that when indiscreetly used or selfishly monopolized the culinary art has encouraged the grossest excesses of man's bodily appetites. Nor is the claim nullified by the evidence

down the centuries that fasting and abstinence, in due season, have encouraged man's highest spiritual and religious development and insight.

Food Technology, Urban Development, Productivity and Leisure

In modern technological development it has been necessary not only to exonerate a large proportion of mankind from the responsibility for food production but also to detach them from the opportunity to obtain on-the-spot fresh food. Were it not for food technology urbanized man would have to subsist on stale and unattractive foods. Canning, freezing and other methods of bulk preservation, supplemented by home refrigeration, have brought far better quality foods to the urban table than were obtainable in the nineteeth century cities.

Moreover, under the slogan "take the housewife's chores into the factory" it has given liberty to women which they are able to plough back into increased productivity or creative arts. The plea that women have not all learned to use their leisure creatively does not detract from the reality of the development.

The physical advantages can be discussed in relation to improvements in health which have resulted in part from twentieth-century food technology.

Technology and Food Variety

Modern technology, through improvements in food preservation and transport, has brought a more complete range of nutrients and more attractive variety of foods to the mouths of greater numbers of people.

Geography, climate and season have already ceased to limit the variety of foodstuffs available to people in developed communities. Tropical, desert and frozen climates no longer impose limitations on the availability of, for example, dairy products, fruits and fresh vegetables. Only the low productivity of labour and associated economic maldistribution maintain any limitations in variety of foodstuffs among under-developed communities. Skimmed milk powder could abolish protein

malnutrition in the pre-school child in tropical Africa if wage structures and custom allowed.

However, coincident with the improvement in quality and quantity of available foodstuffs, there has occurred a population explosion which threatens to neutralize all the benefits in many parts of the world.

We can examine certain changes which have occurred to a striking degree among the privileged nations of the Western world where population has not outgrown the improvement in quantity and quality of available foodstuffs. Among the parameters, two can be measured with sufficient accuracy to be incontestable. These are life expection and stature.

Life Expectation

The evolution of what we call Western civilization has coincided with a remarkable increase in life expectation. Figures produced recently by the Metropolitan Life Insurance Company of the U.S.A. show that this trend towards better expectation of life is still continuing in both sexes, being in the year 1960 an expectation of life at age 5 of 70.7 for white females and 63.8 for white males. These figures are far in excess of comparable figures in the U.S.A. twenty-five years previously and in all but a very few small regions of the world today. Negroes and coloured people in the U.S.A. have an expectation of life at age 5 of 66.2 and 61.9 for females and males respectively. Although it is possible that genetic factors underlie these differences between White and Coloured people, most students of life expectation and morbidity and mortality trends believe that the differences are due in the main to environment. The rôle of socio-economic factors among the total environment is well exemplified in differences between white and Cape coloured people in the Cape Peninsula of South Africa. These two populations have lived cheek by jowl for more than two hundred years in the same climate and exposed to the same infections and other stresses. The only important environmental difference between the two population

groups is that implied in the socio-economic privilege of the whites. Differences in mortality are most striking in the first five years of life (Table I).

Table I

Race	*Death from all causes* *per* 1,000 *live births*	*per* 1,000 *population*	*Death from gastroenteritis as % of deaths from all causes*	
	0–1 *year*	1–4 *years*	0–1 *year*	1–4 *years*
European	23·3	0·9	1·2%	5·9%
Cape coloured	85·69	10	35·4%	40·7%

(Robertson, I., Hansen, J. D. L., and Moodie, A. [1960]. *S. Afr. med. J.*, **34**, 338)

Approximate figures for life expectation among adults of the two populations are:—

Table II

	Whites	*Cape coloured*
Life expectancy at birth (years)	67	47
Percentage poverty	2	33

(Gordon, H. [1962]. Personal communication.)

Human Stature and Body Build

In all Western European countries for which there is reliable information there has been through the first half of the twentieth century a trend towards taller and heavier individuals. These trends are apparent in the U.S.A., Canada, New Zealand and Australia as far back as records go and in Japan, to a slightly lesser extent, at least since 1900. The gain in weight amounts to the equivalent of one year in forty years and in height amounts to 1.5 centimetres per decade or one inch per generation since 1850.

It is recognized that body build is made up of many components affected by inheritance and environment; also that experimental work in animals leaves some doubt as to the eventual advantages of rapid growth in the early phases of life with resultant increase in final body size. These matters are too complicated to discuss at present in relation to human stature and body build.

Food as One of the Causes of Improvements in Life Expectation and Stature

The improvement in life expectation and the increase in stature for which figures have been given can of course not be

attributed solely to improved food. Many other aspects of preventive environment have been improved during the twentieth century, while the therapeutic prevention and treatment of many types of disease has been vastly improved by the advances of medical science. Hybrid vigour has recently been canvassed as contributing towards increased stature. I am going to avoid controversy by confining myself to the conservative statement that, among all the many operative factors, improved quantity and quality of food must have played an appreciable part.*

* If anybody is inclined to contest my dogmatism about the important rôle of food I would meet him with some facts produced by my co-workers in Cape Town. Many public health workers and educators, when discussing infantile gastroenteritis, are inclined to attribute this principally to defective hygiene and to regard the associated malnutrition as a result of the infection. We have strongly suggestive evidence that, among our Cape coloured infants, the malnutrition was present before the gastroenteritis occurred. We believe, therefore, that properly nourished children have less morbidity and lower mortality from infective gastroenteritis and that the most important single measure in combating gastroenteritis in the pre-school child is better feeding.

THE DISADVANTAGES OF SOPHISTICATED DIETS

Many of the advantages discussed in the previous chapter are bought at the price of some inseparable disadvantages. Some of these are overt and indisputable. Others are latently possible, particularly those which may operate covertly over long periods of time to undermine constitutional resistance to degenerative disease. They will be considered in an objective and critical spirit. Reference will then be made to some food fads which have wide acceptance even among educated people, before an attempt is made finally to weigh up the balance of effect on human health of the favourable and unfavourable trends in dietary sophistication.

From a scientific viewpoint the unfavourable effects can be conveniently classified in terms of their early or late effects after consumption of the food.

Immediate ill-effects

These fall under two main headings:

(*a*) Unsuccessful sterilization.

(*b*) Acute toxicity of additives.

The first of these is represented by the immediate effects of preformed bacterial toxins such as those produced by staphylococci, *Clostridium welchii* and *Bacillus botulinus.* These "ptomaine" poisons may occur in naturally-stored foods but their effects may be rendered explosive and epidemic by unsatisfactory canning. With improved public hygiene, especially through household refrigeration, reduction in their frequency and severity will eventually be counted among the advantages rather than the disadvantages of technological sophistication.

The second group is unlikely to occur except through industrial mistakes in the identity or quantity of preservatives added in processing.

Early Effects

The early adverse effects of technological sophistication result mainly from the magnification of the spread of bacterial infection of food by wholesale processing. Meat, milk, eggs and vegetables, infected with salmonellae, are an increasing problem to countries relying on imported foodstuffs. In Britain recorded outbreaks of food-poisoning increased ten-fold between 1938 and 1959. The major factor in this increase has been importation of contaminated foods from abroad, and most of this has been attributable to salmonellae of which seven hundred serotypes are now recorded. Against this debit to technological sophistication must be set the credit of reduction in other food-borne bacterial diseases by public hygiene generally and pasteurization of milk in particular. The balance must surely be on the credit side.

Intermediate Effects

Under this heading the tale of ill-effects of sophistication of foods mounts heavily. The story may best be handled by

taking up certain diseases and unhealthy trends in modern civilization and tracing them back to their major aetiology in sophistication of foods.

Deficiency Diseases from Refinement of Staple Foods. This group of effects is well exemplified by the problem of beri-beri in rice-eating communities. The refining of whole-grain rice leads to the removal of most of the husk and germ in which thiamine (vitamin B) is contained. When rice is the major source of calories in the diet, epidemic and endemic beri-beri result. The story is well reviewed in an FAO report[3] (1954). The interest to our discussion is the tenacity with which the ordinary people of the East adhere to this particular form of food sophistication. Return to "natural" or parboiled whole rice is resisted so strongly on account of taste, tradition and status symbolization that it has proved easier to enrich refined rice with synthetic thiamine.

Very similar tenacity of prejudice has been experienced with the more educated people of Western civilization in regard to white and brown wheat flour. Britain and the U.S.A. have capitulated to public demand and approved a policy of enrichment of white flour with synthetic nutrients which are removed in the process of milling, notably thiamine, niacin and iron.

Caries of Teeth. There can be no doubt about the unhealthy effects of sophisticated diets on the incidence and prevalence of caries of the teeth. The classic example of the experience of the people of Tristan da Cunha in this respect has been duplicated in many parts of the world. The exact mechanism is still obscure but it appears to be multiple. Firstly concentrated foods, such as purified sugar, left in the gingival pockets encourage the growth of caries-producing bacteria. Secondly the reduction of friction on the gums from chewing of hard "natural" foods seems to alter physical conditions in the mouth and so reduce resistance to caries-producing bacteria. Finally it is possible that the acidity and chemical constitution of saliva may be altered, through internal metabolic effects of sophisticated diets, in a direction which promotes caries.

Obesity. This term is used in the sense of increase in the amount of adipose tissue relative to lean body-mass and particularly skeletal muscle mass. It is often, but not necessarily, associated with overweight—the term does not necessarily connote obesity.

The adverse effects of overweight on mortality are adequately documented by insurance statistics. It must be admitted that statistical proof that the direct association between mortality and overweight is due to obesity is not conclusive; this gap in knowledge is due to the practical difficulty of measuring obesity in exact figures. But few critical observers would deny the high degree of probability which is generally assumed. Obesity is also reasonably assumed to be responsible for much morbidity from osteoarthritis and musculo-skeletal deformities, bronchitis and emphysema, diabetes mellitus and hypertension. The statistics of the Metropolitan Life Insurance Company of the U.S.A. have shown that for a man of 45, an increase of 25 pounds above standard weight reduces his life expectancy by 25 per cent [4].

The causes of obesity are multiple and complex. Inability to control appetite and so match caloric intake to energy expenditure is the major practical factor. Here sophistication of foods is a major cause. Natural vegetable foods mostly contain enough cellulose residue to give the stomach a comfortable sense of repletion before calories have been consumed in excess. The consumption of sugar and refined carbohydrates is without this built-in restraint. The culinary art and twentieth-century food technology, including food advertisements, have set endless traps of sight, taste and smell to break down the restraint of appetite. Animal selection and scientific feeding have, through the meat and dairy industries, contributed to raising the percentage of fat calories from 15 per cent or less in primitive agricultural communities to 45 per cent or more among sophisticated population groups. This is conducive to over-consumption of calories.

Constipation. The refining of foods by exclusion, *inter alia,* of much of their natural cellulose has contributed to a widespread

problem of constipation. Although not in itself serious, constipation has led to widespread purgative abuse which has been encouraged by subtle advertising by the manufacturers of aperients. This leads in turn to purgative addiction, secondary dyspepsia and much anxiety and tension. The net contribution to human misery and ill-health is difficult to measure but must be considerable. Admittedly lack of exercise and the tension arising from urban civilization play some part.

Biliousness and Indigestion. Overloading the stomach and perhaps the liver with foods rich in fat and protein is, and has been, an immediate cause of biliousness ever since the food served at banquets became sophisticated. A healthy constitution can cope with periodic insults of this sort, but the twentieth century has brought repeated or even daily exposure to many more people.

Indigestion detracts from the joy of healthful living and causes untold misery, and therefore wrong judgment and action, in sophisticated living.

Many other diseases could be cited which occur with increasing prevalence in sophisticated communities, for example peptic ulcer, appendicitis, etc. Those which have been discussed have been selected because it is believed that the consumption of sophisticated diets plays an important, although not a lone, part in their association with high standards of living. It must be emphasized that most of the remaining causes of morbidity and mortality in advanced communities have complex and multiple aetiology. This thought leads up to the next group of adverse effects—those that operate over long periods of time.

LONG-TERM ADVERSE EFFECTS OF SOPHISTICATED DIETS ON HEALTH AND CONSTITUTION

Much of what is to be said under this heading can be expressed only in terms of probabilities and possibilities. Also, some of it may play into the hands of food faddists, and I am reluctant to expose myself to misquotation or misinterpretation by them. I believe, nevertheless, that it needs to be expressed

at least in hypotheses which should be submitted to scientific investigation.

The obvious favourable effects of twentieth century technological sophistication of food on life-expectation and stature have been examined already. The total is impressive, and any adverse effects have, up to the present, been negligible by comparison. The favourable effects have been largely due to production by farmers of more and better quality foodstuffs, and their more efficient and universal commercial distribution. But it must be recognized that these benefits have been achieved through a technology which has inevitably involved sophisticated methods of production and processing. Admittedly some of these technological methods are capable of improvement in the direction of producing foods nearer to the concept of "primitive simplicity or naturalness".

At the Tenth Anniversary Symposium of the Ciba Foundation[5] I devoted most of my communication on "Research in Clinical Nutrition" to the great advances in our knowledge of protein requirements which have developed out of the public health and scientific study of the deficiency disease called kwashiorkor. At the same time I drew attention briefly to the rapid advances in our knowledge of the rôle of fats in diets with particular reference to ischaemic heart disease.

Fats and Heart Disease. The rising prevalence of, and the increased mortality from, ischaemic heart disease in privileged Western communities, and particularly in the privileged social groups, are statistically associated with changes in total serum cholesterol and other lipid fractions of the human blood including especially triglycerides and phospholipids. These lipid changes, in turn, are clearly related to changes in the quantity and quality of dietary fat resulting from technological food sophistication. Many factors other than diet obviously influence the adverse trends—such as lack of exercise, tension and strain, and cigarette smoking, but there can be no doubt about the significant rôle played by diet in general and by dietary fat in particular. Mechanisms are still obscure and complex but this fact does not detract from the significance of the trends.

Other Diseases of Multiple Causation. Besides ischaemic heart disease there are many diseases of multiple and uncertain causation which increase in prevalence with advancing levels of civilization. Changes in habitual dietary pattern almost certainly play some part, perhaps an important part, in their causation. Diabetes, peptic ulcer and appendicitis can be quoted among many.

Food Additives and Residues. Perhaps the most potentially serious adverse trend in twentieth-century food technology is the incorporation of a great variety of additives into commonly used foodstuffs. They have been classified as follows:—(*a*) food colours; (*b*) preservatives: (i) antimicrobial agents, (ii) anti-oxidants; (*c*) emulsifiers.

Joint FAO/WHO Expert Committees issued a series of reports on food additives between 1956 and 1962.[6-10]

There is a further problem created by residues of chemicals used by plant or animal breeders and found, therefore, both in unprocessed and processed foods. The chemicals include antibiotics, arsenicals, oestrogens, coccidiostats, etc. used to improve the health or accelerate the growth of animals, birds or fish reared for human consumption or for their edible products—dairy products and eggs. Other chemicals, which include a great variety of pesticides, leave residues which may be consumed by man directly in vegetable foods or indirectly when contaminated plants are consumed by animals reared for use as human food.

These residues of artificial contaminants (chemical residues) are sometimes loosely included under the term additives. It would seem less confusing to confine the term " additives " to those chemicals which are added in the course of processing for storage and distribution. The Joint FAO/WHO Committee appears to be following this latter usage in its reports.

Apart from identifiable acute or subacute toxic effects it is possible that consumption of small quantities of these additives and residues over long periods of time might affect constitution in such a way as to undermine health and resistance to disease. These chronic possibilities can be examined under the following

mechanisms which can be reasonably postulated by analogy from experimental studies.

(1) Disturbance of co-ordination and integration in the central nervous system. This possibility was well demonstrated by the late Sir Edward Mellanby in the phenomenon of canine hysteria in dogs fed on bread in which agene had been included as an "improver". No adverse effects from the consumption of this bread by humans was ever demonstrated but agene was rightly banned.

(2) Carcinogenesis: The possible carcinogenic effects of additives in food processing was the subject of a special report[9] by the Joint FAO/WHO Committee in 1961. The testing methods recommended by this Committee need to be applied to the quantities of residues of oestrogens and other potential carcinogens which are found to be present in unprocessed animal flesh and products used for human consumption.

(3) Disturbance of endocrine balance through the consumption of oestrogens and other endocrine growth promoters incorporated into the flesh of poultry, calves and other animals reared for human consumption, or into dairy products[11]. It would seem unlikely that they would be sufficient to promote ill-health through this mechanism provided the feeding of the oestrogen to the animal is discontinued for two or three days before slaughter. However, the practice of implanting steroid hormones may require further quantitative assessment.

(4) Sensitization of the body to antibiotics and oestrogens used for the same purpose in the meat, poultry and dairy industries. Allergic reactions apparently traceable to penicillin in dairy products have been reported both in Britain and the United States[11].

(5) Cirrhotigens. The possible contributory effects of natural contaminants in the production of endemic cirrhosis of the liver have been considered with special reference to alkaloids from the genus *Senecio* but this mechanism has not yet been discussed in relation to food additives or artificial residues.

This account of some of the potential hazards resulting from the increasing use of artificial additives in food processing and

of chemicals in the sophisticated culture of plants and beasts may sound very alarming. The reports[9] from the Joint FAO/WHO Expert Committee on food additives and a symposium organized in 1961 by the American Journal of Clinical Nutrition stand witness to increasing uneasiness on this score[11].

It would be reasonable to adopt a strict approach to those additives which serve no useful purpose other than improving appearance or flavour. Food colours could reasonably be banned until they have been thoroughly tested according to principles laid down in the reports of the Joint FAO/WHO Committees.

On the useful additives and chemical residues we must keep a proper perspective. Almost every aspect of modern technology has introduced new hazards into our environment. Food technology is no exception. I quote from one contributor to the symposium in the American Journal of Clinical Nutrition:

> Should we not try to determine whether the hazard is large, medium sized, small or imaginary? In every decision on additives and residues, concern for the public health must be paramount; but if the risk is so small that it can be appreciated only by the elect, the professional viewers-with-alarm, then at least it should be balanced against the economic advantages of the additive in question. In considering the problem of residues, let us not lose sight of the importance of the protein and vitamins which we expect producers to furnish us at low cost in meat, milk and eggs.

Metallic Contaminants

Technological sophistication has introduced into the diets of man small quantities of metals and trace elements and if these are not excreted there is a possibility of extensive accumulation during a lifetime.

One example of this is the accumulation of iron in the tissues of the Bantu of Southern Africa. The exact reasons for this accumulation are still unknown. Possibilities include the effects of malnutrition on the metabolism of tissue cells (cytosiderosis) and increased absorption of iron from the intestine in pancreatic deficiency. Another reason, undoubtedly, is a high intake of iron in the diet derived from customs

of cooking and fermenting in iron pots. In terms of the introductory paragraphs of this article, the replacement of earthenware pots by iron pots, even among a primitive people like the Bantu, may be regarded as an example of sophistication of diets. At a more advanced level of cultural organization, there has been considerable speculation about the possibilities of aluminium poisoning from the use of aluminium saucepans. In twentieth-century technological sophistication the extensive use of tin cans for the storage and transport of foodstuffs has introduced further possibilities for trace element accumulation.

FOOD FADDISM

Food faddism goes back a long way in man's history[12]. It is inevitable that the technological sophistication of the twentieth-century should be countered by back-to-nature faddists. These fall into several broad groups including: (1) Those who advocate as little processing of foods as possible. (2) Those who believe that artificial fertilizers for vegetable crops are inferior to natural humus. (3) Those who advocate taboos on one or more foods which are regarded by scientific nutritionists as healthy, e.g. vegetarians and vegans. (4) Those who believe that certain combinations of foods are unhealthy while the same foods are healthy when consumed at separate meals, as in Hay's Diet.

A few comments on these four groups of food fads may be in order.

(1) The objections of the first group have been dealt with in the rather full remarks in this paper on the respective advantages and disadvantages of technological food sophistication. This cult provides, however, a useful corrective to the enthusiasms of commercial food entrepreneurs. (2) The supporters of natural humus against artificial fertilizers have, in essence, a case which would be accepted by most scientists if it were restated not as a mystique, but in scientific terms of specific nutrients, such as trace elements, missing from the soil. (3) The case propounded by vegetarians and vegans appears to the writer to be based mainly on considerations other than those of

physical nutrition and health, grounds which can perhaps be described as "humanitarian" although the term is inept. From the nutritional point of view there is no doubt that when dairy products and eggs are included, an otherwise mixed vegetable diet can be entirely healthy. The evidence is almost overwhelming, however, that strict vegetarianism (veganism) is incompatible with healthy human development. (4) As a physician I am satisfied that those who follow diets such as those advocated by Hay often obtain great benefit. This benefit is undoubtedly in part the result of suggestion and in part the result of healthy simplification of diet by those who have been over-indulgent of themselves. No satisfactory physiological evidence has been brought forward to support the basic tenets underlying this food fad.

Non-Physical Disadvantages

To the real or supposed disadvantages of dietary sophistication can be added some unfavourable effects which constitute part of the total stresses exerted on man's psyche by urban technological development. According to Trémolières, the French, for example, see in food technology a threat to family life and culture through a resultant decline in the culinary art and its associated cultural values. They stress the importance to the family of the mother's rôle in purchase and preparation of foods leading up to the family gathering at the principal meal.

SUMMARY—THE BALANCE OF EVIDENCE

The varieties of sophistication of foods which can be traced in man's history have been classified and contrasted with twentieth-century technological sophistication to which the major part of the discussion is devoted. The cultural values of eating are stressed.

The catalogue of physical advantages experienced by Western civilized man during the twentieth century is impressive. These advantages have been won in part through improved quantity and quality of foodstuffs made available

to the ordinary man. This technological sophistication has entailed some potentially dangerous trends which will need to be carefully watched. These include certain vitamin deficiencies; caries of teeth and orthodontic problems; unfavourable morbidity and mortality experience from ischaemic heart disease, resulting from changes in quality and quantity of dietary fat; similar adverse trends in the incidence or prevalence of other diseases of multiple causation such as diabetes, peptic ulcer, appendicitis etc. ; and the possibility of chronic poisoning and even cancer from food additives and chemical residues in food.

The claims of back-to-nature and other food faddists are found, when critically examined, to have few substantial bases.

Finally, the non-physical advantages resulting from the increased productivity and leisure of urban development have been made possible by twentieth-century food technology, which is inevitably sophisticated in the sense defined.

World Resources

DISCUSSION

Wright: I take it that the value of this symposium is to reveal, and if possible to reconcile, differences of viewpoint; and in this respect I must own that I am frankly disappointed with Professor Brock's contribution, for I find little if anything to quarrel with in it! On the other hand, Colin Clark has lived up to his reputation, if I may say so, of providing material full of controversial issues. There are so many, indeed, that I hardly know where to start.

I should first like to point out what I believe to be three factual errors in the figures presented to us. These might appear to be of minor significance, but if one can make mistakes in minor facts then one can make mistakes in major facts. In this connexion I should like Colin Clark to know that every figure that I am going to quote here has been objectively arrived at and has in fact been checked by my colleague Dr. Sukhatme, who was commended by Clark himself for his objective outlook.

Clark said that if agricultural products are converted (by means of their relative prices) into grain equivalents, and some margin is allowed, minimum requirements can be stated as approximately one quarter of a ton of grain equivalent per person per year—that is, about 250 kilograms per annum. Now as it happens, we have just completed in FAO the Third World Food Survey, which I hope will be published in the course of the next month or two, and my colleagues have recalculated the needs of the underdeveloped countries. On this basis, using the FAO Report on Calorie Requirements to which Clark has referred, it works out that in the underdeveloped countries the average requirement is 2,300 calories per person per day at the retail level, which is approximately 240 kilograms of net

grain equivalent, or roughly Colin Clark's figure. To this, however, must be added—and I think Clark omitted to do this—losses in extraction which amount to about 20 per cent, and losses due to non-food use, such as seeds, in manufactures, and also storage losses, which together account for about a further 15 per cent. Therefore Clark underestimates the grain equivalent at production level—and this is the important point—by between one-fifth and one-third. Thus his estimate is 250 kilograms as against 300/350 kilograms in practice. Now this is a considerable discrepancy for the underdeveloped countries where agriculture is difficult; and, most important, Clark's figure makes no allowance for minerals and vitamins which he rightly holds to be essential.

The second factual error is the statement that a person's minimum requirements for a year can be grown by any good farmer on 600 square metres. The present world output is about 500 kilograms of grain equivalent per hectare of agricultural land. Now if we assume my minimum figure of 300 kilograms to be necessary, we should require on a world basis three-fifths of a hectare or 6,000 square metres. The world average yield per hectare would therefore have to be increased ten-fold above the present level in order to reach 300 kilograms of grain at production level from 600 square metres. Phenomenal increases can be obtained in agriculture in certain areas, but a ten-fold increase is surely too much to expect universally in the foreseeable future and certainly needs more emphasis than saying that "it can be done by any good farmer".

The third point is that even in the Far East we are already producing 340 kilograms of net grain equivalent per person per year, which corresponds to about 450 kilograms at the production level. Thus nearly double Clark's figure is already available in the Far East, and yet there is substantial malnutrition as well as under-nutrition in this region today, which the existing rate of production is apparently incapable of meeting. I would prefer to leave it to Brock and to Trowell to discuss the general question of the extent of malnutrition because they

have worked in the areas concerned and can give us first-hand views about it.

Incidentally, the figures based on our Third World Food Survey which is about to be issued show that we must aim at a target of a ton of grain equivalent at the production level per person if we are to eliminate both under-nutrition and malnutrition, which is more than twice the present figure.

May I now turn to consider our present and future position? The latest calculations based on FAO's Report on Calorie Requirements indicate that 10 to 15 per cent of the world's population is undernourished in the sense of not having sufficient calories, a figure which I think Clark has stated both here and elsewhere to be probably an underestimate. Personally I would tend to agree with him, but for a different reason, namely that I consider that calorie requirements must be dynamic and not static. We cannot necessarily expect a 50-kilogram man to remain at 50 kilograms if in fact his low weight is due to under-nutrition or malnutrition and not to genetic influences. So I agree here with Clark that a figure of 10–15 per cent or even 20 per cent of the world population represents the under-nourished.

But the problem of feeding the world adequately is not simply a question of supplying calories. The widespread occurrence of deficiency diseases indicates that there must be improvements in the *quality* as well as in the *quantity* of the diet in many areas. Now here I think we come to the crux of the problem. How do we supply the vitamins and minerals which Clark rightly acknowledges to be necessary? Clark dismisses somewhat airily, if I may say so, the value of animal protein as the reasonable index on which to base quality improvement in the diet. It is, of course, true that there are proteins of plant origin of relatively good quality, but it is necessary to provide for a suitable mixture of them, from different grains and from different pulses, to get an adequate supply of amino acids, which is probably as difficult, if not more difficult, than supplying animal proteins. There is moreover no doubt that the supplementary values of amino acids from animal products are more

satisfactory, most certainly for children and other vulnerable groups within the population. I cannot, therefore, accept the contention that animal proteins are now virtually shown to be of no greater value than plant proteins.

Moreover, the emphasis placed by myself and my colleagues in FAO on increasing the consumption of animal products is more widely based than on a mere consideration of the value of animal protein *per se*, important as this may be.

In the first place, the passage of plant food through the animal not only results in an improved quality in the food constituents, which resemble more closely in pattern those constituting the human tissues, but these constituents are present both in far higher concentrations and in more readily available form than in plants. For example, the protein content of dried grass varies between 10 and 20 per cent, whereas the protein contents of the solids of milk, cheese and eggs lie between 30 and 50 per cent. As regards fat, the dry matter of plant tissue seldom exceeds 5 per cent; indeed in most cereals it is about half this figure. In the solids of milk on the other hand it is 30 per cent, in eggs 40 per cent, in cheese over 50 per cent, in meat sometimes more than 60 per cent. The increases in the concentration of nutrients apply equally to vitamins and minerals.

In the second place—and here I am speaking as an agriculturist—animals do not in general compete with man for the same portions of the plant. In the United Kingdom, for example, grass provides 60 per cent of all nutrients for livestock. In India, to take another extreme example, dry and green fodder crops provide 95 per cent of the whole of the animal nutrients. In Africa there are many semi-arid zones where one can only adopt nomadic grazing. In deserts there are places where man, in the absence of available water, has in fact to rely on his sheep and goats, grazing nomadically, to provide him with the necessary water in his milk.

As regards the extent to which other crops are consumed by animals, livestock eat, on the whole, the straw, the milling offals, the by-products of the oil-seed crushing industry, the tops of the pulp of sugar beet, and slaughterhouse offals—all of

which are inedible by man; they even eat brewer's grains in order that we can enjoy our beer! So animals do in fact constitute a very valued means of utilizing the by-products of our agriculture, rather than robbing us of agricultural produce, except in the very highly developed areas.

In the third place, and I hope Pirie will bear me out in this, animals play a valuable rôle in increasing soil fertility, and in this way help to conserve the natural resources of the land, either by providing farmyard manure or more fundamentally in the system of mixed farming which is being increasingly adopted to improve the food crop production in the less developed countries.

In the fourth place, the level of animal protein in a diet can in any event be looked upon as a convenient *index* of the general level of quality of the diet, since it serves as a general indicator of poverty or wealth. The whole diet is probably better where there is a higher consumption of animal food.

Finally, in the fifth place, how else can we hope to ensure the presence of the necessary vitamins or minerals than by providing a mixed diet with animal products? And must we not also pay some attention to palatability? Julian Huxley asked us "What are people for?" Surely we are not here merely for existence; people do have a right to enjoy the food they eat! Palatability itself is indeed vital in any diet. Colin Clark himself, in an article in the Dutch press, has said "It is true that to most of our fellow men this [a cereal diet] means a monotonous diet, consisting mainly of cereals. We all look forward to the day", he adds, "when they, as well as we, are able to include in their daily menu more meat, fruit and dairy products." It is, I think, significant that all better-off nations automatically change towards a diet with more animal products, more animal proteins, more fats—a useful form of concentrated energy particularly for industrial workers—and more fruits and vegetables.

If my thesis is correct, animal foods do therefore form a useful index not only of the physiological quality of the diet, but equally of the order of magnitude of the effects of specific deficiency diseases, of the extent of satisfactory health and

activity, and of what I would term the better life for which so many yearn.

On the basis of the two indices afforded by calories and animal protein FAO's Third World Food Survey has arrived at a figure not merely of 10 to 15 per cent of under-nourished people due to caloric deficiency, but reaching up to 50 per cent of the world's population if one takes into account those who are *either* under-nourished *or* malnourished *or* both. Some of my nutritional colleagues consider that even this figure is an underestimate.

I would end by indicating the impact of FAO's Third World Food Survey on the future needs of growing populations. The United Nation's median estimate is that by 1975 (only 12 years from now) the world's population will have risen from roughly 3,000 million at present to about 4,000 million. For this we reckon, and these again are Dr. Sukhatme's figures, that we shall require on a world basis 50 per cent increase in total foods and nearly 60 per cent increase in animal foods. In the underdeveloped countries this latter figure would be doubled, that is to say, an increase of 120 per cent, even allowing for only a modest rise in the consumption of animal foods. By A.D. 2000 when it is estimated that the population will have risen from 3,000 million to over 6,000 million, total foods will have to be increased by 170 per cent and animal foods by over 200 per cent, this latter figure being increased in the underdeveloped countries to nearly 500 per cent, or six times the present figure. In the light of these figures and knowing the difficulties of increasing production in the underdeveloped countries, I must own to being sceptical of Clark's optimistic view that the population which we could cater for in the future would be far in excess of anything we contemplate now. In any event, can we realistically assess the needs of a period beyond A.D. 2000, with all its uncertainties?

Clark: Many of the best farmers in Britain are now turning away from mixed farming. They have some backing from the soil scientists who say that livestock is not necessary so long as one looks after and fertilizes the soil carefully—certainly the

economic case is for more specialized farming. I would indeed like to see everyone have a lot more animal protein, but you have not proved that it is physiologically necessary. I cannot debate the Third World Survey which has not yet been published, but it does not prove that we could not manage with Pirie's grass proteins instead of animal protein if we had to. I do not say that we should do so, but I would like to know what the physiological minimum is.

In the same way I can hardly debate your point that we need a ton of grain equivalent per person per annum because you have not produced any evidence for it yet. I should have thought my meaning was quite clear when I said that any good farmer can produce this requirement on 600 square metres, that is to say at the rate of 4 tons per hectare, which is the yield of cereal farming in the United States or alternatively of land cultivated in Japan. Incidentally the Japanese keep their soil in extremely good shape without having any livestock at all. I put in no allowance for wastage, because I assume that people who are really short of food will take care not to waste it. I am, of course, well aware of the needs for seed, and also the danger of losses in storage for which quantitative values are very difficult to place.

Trowell: Speaking as a clinician who worked in under-developed areas of Africa I feel that the figure for the under-calories group of 10–15 per cent of the population is fairly realistic, but in Africa we see only seasonal under-nutrition and very seldom, apart from civil disturbance or warfare, anything like the serious calorie shortage which I understand occurs chronically in the East. What happens to people who are permanently short of calories? Do they go down continuously in weight or do they just do less and less work? We still lack basic clinical studies on this problem. In Africa, the best studies have been carried out in Gambia where there is seasonal under-nutrition, particularly towards the end of the dry season and beginning of the rainy season. Before the new crops come in, body weight drops and activity decreases; then after the harvest, the people feed up again and become more active. This type

of underfeeding, a seasonal shortage only, might reduce the figure of 10–15 per cent who are thought to get too few calories throughout the year.

With regard to protein—a subject which has interested me from a paediatric point of view in the tropics—so far as I can see the question of whether 50 per cent of the world is poorly fed still turns basically on the larger figure of 30–40 per cent for protein malnutrition. The evidence very largely hinges on the fact that children in the underdeveloped areas do not grow as fast as they would if you improved their diet or as fast as their counterparts, the coloured people in the United States, grow. Secondly, the serum proteins in their blood show quite abnormal figures which are altered by improving the diet. Thirdly, from a very young age after weaning, the liver structure shows an abnormality in the opinion of practically all the best pathologists who have examined the question. That is to say, the majority of cases show an increase of cells and reticulin structure about the portal tracts in the liver. We have also got to remember that on what might be called the under-developed type of nutrition as seen in Africa certain diseases are rare, but others are common. Two of the relatively common conditions found in Africa are endomyocardial fibrosis, rarely seen in advanced countries, and periportal fibrosis of the liver and perhaps also primary cancer of the liver. On the other hand some diseases which are very common among those who eat high-grade diets are rare in underdeveloped countries. Thus coronary heart disorders, vascular disease of the brain, gall-stones, rheumatoid arthritis, osteitis deformans and disseminated sclerosis are rare in Africans in Africa, but not among their better-fed cousins in the United States. There has always been a tendency to set nutritional standards high, to fear deficiency and to discount excess. But we still lack satisfactory longitudinal studies in man of the end results of diet. I fear that we are giving our own European and American children too much; at the same time we are exaggerating the figure of 30–40 per cent for protein malnutrition in the world. At a guess I would halve this figure.

I should also like to draw your attention to the incidence of certain forms of carcinoma in groups matched in sex, age and size, from the United States on the one hand and Africa on the other. This really does come down to something fairly fundamental. The coloured folk of the United States came largely from West Africa and are predominantly Bantu, although possibly they have some genetic variation from those in South Africa. An excellent carcinoma survey was carried out in Johannesburg, from which the ratio of liver cancer in Africans was found to be about five times as frequent as in American negroes, but curiously enough the gastrointestinal tract showed less cancer in Africa. I suggest that this is best explained in terms of the end results of a certain diet rather than climatic and genetic variation.

Is there any difference in the internal chemistry of the tissues of Africans as compared with Europeans? So far as I know no difference has been demonstrated at birth. Consider the figures for two groups of adult men (African and European) matched in age. All had been resident in Johannesburg and were examined by the same method at the same laboratory. European men had a higher serum albumin and a lower globulin than Africans; this was due to chronic disease of the liver in the latter group. Africans had far lower blood cholesterol and broke up clotted blood more quickly than Europeans; this ties up with less coronary heart disease in Africans. Similarly there were other differences in some of the hormones such as 17-ketogenic steroids and oestradiol. Other workers have reported changes with respect to magnesium, iron, copper, and protein-bound iodine. The suggestion is that diet alters the internal chemistry of the body, which is not as constant as physiologists have assumed. One pattern of internal chemistry predisposes to one set of diseases but protects against another.

Which is the better dietary regime, the African or the European? Perhaps we cannot answer that question while we disregard environment. We have come to understand the complexity of value for survival of certain aspects of genetic inheritance but we have not taken the corresponding step in

dietetics. Thus it is an advantage to have one sickle-cell gene if one grows up in a malarial country, but not elsewhere. So far as I can see the best diet is intermediate between the advanced European and the rather low African. In fact we may find that there is no such thing as a good or bad diet, but that there are certain dietary ranges that produce certain types of disease pattern, particularly later in life. If this idea can throw any light on the chronic degenerative diseases of Europeans we shall feel very much rewarded, for at present neither cause nor cure is known. I should not like any of these rather heterodox ideas about diets and degenerative diseases to be taken to contradict what I believe is a fundamental fact, namely, that many young children in underdeveloped countries do not get enough protein—and animal protein plays a very important part in this. Similarly many adults in such countries are from time to time short of calories.

Brock: Clark has challenged those of us who are interested in clinical malnutrition to produce evidence that there is widespread malnutrition. I believe that certainly so far as the African continent is concerned the figure of 10 to 15 per cent incidence of undermalnutrition is fair enough, although I suspect, as Trowell does, that in the Far East it is higher. Secondly, I believe that human nutrition experts have put forward ridiculous figures for some nutrients in the recommended allowances. The most obvious one is calcium, which is given by certain American tables and most international tables as 800 milligrams per day, whereas we know that in South Africa the Bantu live and develop normally on 300 milligrams per day and even have more heavily calcified skeletons than the Europeans living on 800 milligrams. The other big fault in these international figures is the vitamin C requirement of 75 milligrams (U.S.A. standard). Certainly the appropriate figure is nearer 50 than 75, even if one allows a one hundred per cent margin over basic requirement.

But at that point I must part with Clark and challenge his estimates of protein requirement, particularly in terms of grain equivalents. I agree that by a judicious consumption of

expensive vegetable proteins which will include pulses and nuts it is possible to construct a diet which is very nearly satisfactory. But I have two pieces of evidence on the requirement of animal protein. First, starting with the International Nutrition Congress in 1953, there has been a series of papers published on vegans, that is to say, people who are vegetarians to the extent that they will touch no animal products. Everyone agrees that a simple lacto-ovo-vegetarian diet is perfectly healthy, but I think the evidence is absolutely incontrovertible that there is a serious deficiency of vitamin B_{12} in the diet of all vegans.

Secondly, various groups have tried in the kwashiorkor context to determine the minimum amount of animal protein which is required to be added to predominantly cereal diets or whether in fact it is possible by mixing a variety of vegetable proteins to produce a food which is healthy for the post-weaning child. For those who are not familiar with this terminology, kwashiorkor is the most serious expression of protein malnutrition that we know: it is a very serious disease indeed which is invariably fatal if it is not corrected with suitable diet. Cure can be initiated in children with kwashiorkor if they are fed a purely vegetable diet, but it cannot be consolidated; such a diet cannot restore them to health. The nearest approach to this was made by the Scrimshaw group in Guatemala who devised a product known as "Incaparina" consisting of several vegetables mixed together. They claim that this purely vegetable diet is adequate for the maintenance of the post-weaning child. I am not convinced about this, however, because our own evidence does not support it. We find that we can maintain or restore health if we add to the vegetable diet a 10 per cent admixture of fish meal or an 18 per cent admixture of milk protein skim-milk. So far as we are concerned we are able only to initiate cure with the vegetable diet, but we are not able to consolidate cure until we put the animal protein in.

Clark referred to unidentified nutrients and in effect challenged us to name them. They are, of course, certain of the essential amino acids. Looking forward to the future of man, there should be no difficulty in producing calories enough for

a very much larger population than we have in the world today. But I think it is going to be extremely difficult to get agriculturalists to increase their production of protein at a rate even commensurate with the present extrapolated rate of world population increase. The limiting factor is undoubtedly protein and this means, in effect, a small group of essential amino acids which the body cannot form for itself, but which it must get in its diet. These include lysine and trytophan, but there are, of course, others.

Clark: Lysine can be synthesized.

Brock: There are a few amino acids which can at present be synthesized economically but lysine is the only one for which this can be done at anything like a realistic figure; indeed most people feel that even the figure for lysine is still completely unrealistic in relation to world needs. The vitamins, the minerals, and the trace elements are not going to present any problem because we will be able to synthesize them all, but I think some macro-elements, particularly calcium, are going to be very difficult to supply through vegetable diets. The amount of mineral fertilizers which will have to be put into the leached-out soils of the tropics in order to raise productivity is fantastic. I am talking outside my field here, but that is how I understand the position.

Lederberg: Which are the amino acids which are most critical for supplementing vegetable protein?

Brock: Lysine and tryptophan are among the most critical but it varies from vegetable protein to vegetable protein—in maize particularly lysine and tryptophan.

Lederberg: Can you tell us the cost of producing synthetic amino acids?

Brock: I do not recall the actual cost; it is quite cheap as amino acids go, but very expensive as nutrients go.

Pirie: Like everyone else who has spoken, I cannot agree with Colin Clark's first thesis, namely that the world food shortage is really a figment of Boyd Orr's imagination, but I think that he is right in his contention that very much more food could be made than is in fact produced. What people

ought to realize is that to get this food will mean spending money on perhaps one-tenth of the scale needed to get to the moon, and if we got our priorities right and spent money in this way it would involve a major agricultural and scientific revolution.

Brock has mentioned "Incaparina", the protein of which is based mainly on cottonseed. Emphasis ought to be put on groundnut residue, soya residue and coconut residue, all of which added together would supply about one-third of the world's present protein needs, if they could be introduced into human feeding. Apart from this work by Scrimshaw, some research going on in Mysore and elsewhere on the groundnut, and the traditional Japanese techniques with soya, this possibility has been grossly neglected.

In the figures which Clark quoted for high yield, he mentioned corncockle and water hyacinth. The troublesome thing about these high yields is that they so often occur in crops for which nobody has any immediate use. Suppose you harvested this vast amount of corncockle, what are you going to do with it? One thing might be to give them to me to see whether I can produce an edible and palatable product from them. Leaf protein, unlike the vegetable proteins which Professor Brock and Norman Wright tended to lump together, is not strictly comparable with the storage protein of seed. It has an amino acid composition much more like that of an animal and this is reasonable because it is a mixture of about 1,000 different enzymes; it is a metabolic functional part of the plant, like liver. *A priori* one would expect it to be, for statistical reasons, a good protein. The results we have obtained so far, and they are borne out on pigs, suggest that it is as good as fish meal. Baby-feeding experiments show that a diet of 50 per cent milk and 50 per cent leaf protein is almost as good as milk alone. I would not claim that leaf protein is as good as milk or should be used on its own, but as a method of stretching an inadequate animal protein supply I think it has great potentialities.

I must say that Clark is entirely wrong if he thinks that by supplying the world's needs for food all arguments about

contraception would be ended. One wants a family of a particular size for its own sake, regardless of the question of feeding it. This is a fundamental point which probably makes me more damnable in this view than if I were to accept contraception as an unfortunate necessity. Even if we could feed all the people, we would still need the ability to control reproduction.

Parkes: If I understand Colin Clark correctly, he said that the cultivable land area of the earth would support 45,000 million people. I wonder what that implies in terms of population density?

Clark: Half an acre each, in the temperate lands, nobody in the polar or the desert regions, but there would be only one-sixth of an acre each in the tropics. Half an acre each means roughly 1,000 people per square mile.

Pirie: That is the population density of Hertfordshire now.

Hoagland: I understand that Holland has 900 people per square mile.

Pirie: Bermuda has 2,000 people per square mile and people go there quite voluntarily!

Clark: Yes. We will grow short of recreational space long before we run short of food. We are only just beginning in England and Holland to think more of our recreational space than of our agricultural space. It will be several centuries before we experience any major pressure on land.

Lederberg: You underestimate the force of exponential growth! If there are going to be 6,000 million people by the end of this century and if there is logarithmic growth with a doubling time of 30 or 40 years, we shall reach your figure of 45,000 million in a single century.

Clark: At the world's present rate of growth of 1·8 per cent a year it takes about 40 years to double the population. The 15-fold increase to 45,000 million would take a century and a half, at this rate.

Hoagland: The arable land will be decreased rapidly because of this doubling of the population every 30 or 40 years. In that period we shall also have to double all our highways, double all our institutions and buildings, our towns and villages,

and this is going to cut into agricultural land considerably.

Parkes: Can you live on half an acre and do everything else on it, including getting rid of your sewage?

Clark: With some difficulty, yes.

Haldane: I would like to quarrel with Clark's remark that the vegetarian diet of Southern India is dull and uninteresting. In my opinion there are three centres of the culinary art in the world, one in France and Italy, of which we are at the margin, one in South China, and one in South India. The latter cuisine is the only one which is mainly vegetarian, and you cannot appreciate it until you have had no meat and fish for a month or two, when you begin to see what these people are getting at aesthetically. It is, in fact, far from dull and uninteresting. Although I am inclined to think you can live well on vegetables alone, I don't do so myself. I have an egg a day (for breakfast) in addition, and when I was in Bengal I also had curds.

I should also be interested to know why Clark thinks the caste system is any more of a handicap than various other economic systems which exist in other parts of the world. It means that the sons of farmers remain farmers, and not very much more than that in the present context.

Part of what is wrong is that agricultural research is extraordinarily conservative, inefficient, and rather corrupt. Medical research is less so, and zoological research less so still. We have got to realize that problems of tropical agriculture have to be worked out in the tropics and not by imitation of what has been done elsewhere. My colleague S. K. Roy finds that if you grow mixtures of different strains of rice in alternate rows, as often as not you will get a lower yield than with either of the varieties when grown separately. But there are cases where you get increases of anything from 10 to 25 per cent per year in the joint yield, repeated over several years. I suggested this work to him on the very simple principle that on the whole tropical plant communities are much more complicated than temperate ones, and you would expect to find more favourable interactions if you looked for them. A second example is even more surprising. Coconut palms have right or left foliate spirals;

the difference is not inherited. T. A. Davis finds that left-handed ones give 21 per cent more in nuts per year than right-handed ones. This would be a lunatic thing to search for; but if you find it you find it, and I think that a few lunatics let loose to look for ridiculous things like that might uncover some interesting facts in 4 or 5 years.

I would finally add that I have seen water hyacinths being grown as pig food in Singapore. Chinese pig breeders use the water hyacinths along with urban food waste, and I don't think they do it out of altruism for pigs, but because it pays them.

Brock: As I see it, the final limiting factor in the feeding of the world's population is going to be a small group of essential amino acids, which of course can be converted into protein equivalents. This will probably represent much less than the recommended allowance of, say, 70 grams of protein per day for the adult, or one gram per kilogram of body weight. When you get down to a pure amino acid diet, you can satisfy the requirements of man on something like the equivalent of 30 grams of protein or probably even less than that. For a child you have to start with 3 grams per kilogram body weight for infants and then work down with advancing age to perhaps half a gram per kilogram for the adult—provided, of course, that this is what we call first-class protein containing an adequate balanced quantity of essential amino acids. It is clear that over a large part of the underprivileged world the protein available for the pre-school child is seriously deficient even for the present population.

Crick: I wonder if we cannot find mutants which will contain a bit more lysine and tryptophan. How many proteins are there? How many mutation events would you need to obtain an adequate amount of lysine and tryptophan in maize?

Pirie: Fowden has published figures on maize from Uganda, showing an extremely wide variation in the methionine and tryptophan content but lysine was always low.

Hoagland: Maize has been cultivated so extensively and in so many different breeds from the wild form that it is very

difficult to know what you would get if you tried to select for lysine or any other essential amino acids.

Pirie: Some strains of maize are quite rich in methionine—they are up to 3·5 per cent, so a mixture containing some maize could probably be made to give an adequate balance of essential amino acids.

Crick: What about microbiological treatments? Do they convert a substantial amount of protein into microbiological protein, which is possibly higher in essential amino acids?

Pirie: They are no higher; but why convert protein into protein? Most of the yeasts and micro-organisms will grow on carbohydrates and inorganic nitrogen.

Crick: I suggested it because I thought you found that the microbiological "protein" tasted better!

Lederberg: If you are talking about a requirement of something like 1 gram of an essential amino acid per day, as a rough order of magnitude, then looking ahead something like 10 to 20 years, do you think it unlikely that chemical synthesis will be able to furnish such materials at a cost commensurate with the need?

Pirie: Synthesis should certainly be an economic proposition, but why bother? Biological systems do it quite efficiently. I see no reason why a factory should be preferable in the long run. In principle, a mixture of maize, as a calorie source, with leaf-protein as a protein source, ought to be about right. Nobody has tried to see whether theory and practice agree. We have been making leaf-protein starting from materials such as pea waste normally discarded in the process of quick freezing green peas. Because I agree with Colin Clark's strictures on porridge, we have also gone into the question of presentation of our leaf-protein on the table. I regard eating as something different from stoking; so we go right through from processing the crop to presenting the product at table.

Hoagland: What percentage yield do you get per ton of leaf?

Pirie: We get about 50 to 70 per cent of what is present in a good leaf. The percentage recovery falls as the initial protein content of the leaf falls. We have made several types of press

for obtaining the juice and tried many different leaf species.

Brock: Do you get rid of the chlorophyll that comes out in your juice?

Pirie: It can easily be done by solvent extraction but why bother? It is quite harmless.

We cook the curd by, for example, placing about 2 grams, mixed perhaps with a little mashed banana, in small patties, which are then fried. Three of these per day meet 10 per cent of a normal person's protein requirement. They are eaten avidly by my staff—they sometimes manage to eat the lot before the visitors, for whom the cooking was being done, arrive.

Crick: How many people would one of your presses supply, if it were running continuously?

Pirie: A machine fed with reasonably moist leaf containing 20 per cent protein (on the dry matter) at one ton per hour for 8 hours on 300 days in the year, would provide about 10 per cent of the protein requirement of 30,000 people.

Crick: So the capital cost per head is really quite small?

Pirie: Yes, the capital cost of a big machine is about £2,500 including the essential pumps, tanks, etc.

Lederberg: What raw material is there that is suitable for this in relation to other food supplies? What increment of our total available food would this represent?

Pirie: We use ordinary agricultural crops because if I used anything else, I'd have to grow it myself. These are not, of course, the ideal plants to use; if one were using the process economically, one would use much leafier crops than these. Ideally one would use some waste product—sugar cane is attractive. I have made protein out of sugar cane: whether it would be economic I am uncertain; it is awfully tough stuff, and its protein content is low, so that you have to do a fair amount of work to get out the protein. Other plants that interest me are sweet potato, ramie, and jute because the leaves are by-products.

Hoagland: Is there no interest on the part of the Indian or other governments in regions where there are food shortages,

in setting up plants to develop this process and investing capital in it?

Pirie: Yes. They have a machine in Lucknow, which is run by the Scientific Research Council. The Indian army also sent a man to work with us for three weeks, and he has written to say that he is building a machine—when it will be finished, I don't know.

Hoagland: One might think you would have a number of orders for these machines and that they would be in demand in a number of places, with the level of yield that you are getting.

Pirie: Well, you live in an ideal world!

Wright: I think this was the experience of Thyssen with food yeast, wasn't it? He could produce food yeast, but he couldn't get it utilized except through very special channels. He did indeed try on one occasion to get the Ministry of Food to utilize it when we were short of protein after the second world war, but the problem was to decide what to put it into. Thyssen had got as much as he could put into a number of Colonial institutions—hospitals, and so on—where people had to take it, but it was not possible to persuade people to use it in the villages.

Pirie: It always seemed to me that that was not very well handled. If someone writes to ask for protein, it is almost always a mistake just to send some. I invite such people to come to see it cooked. If we can show them how to handle it, then they go away convinced that it can be done. Otherwise, even able cooks become discouraged at their first efforts. Because it is an unusual thing to cook with, people won't try, and that is so with yeast too. If you make these patties with banana in them and so on, then people eat it. That is what Thyssen failed to do.

Wright: He tried to use it in biscuits and in bread. He certainly tried a number of different vehicles for it, but none of them was ultimately taken up anywhere. So far as I know, the plant is not producing at all now; it has even, I think, been dismantled.

Price: Can I ask as a layman if these biochemically natural foods might have unfortunate side effects, like the artificial additives? Have any screening tests been made?

Pirie: No. One eats quite a lot of leafage in various forms already, without, so far as I know, any side effects, nor are they to be expected. But there are goitrogens in cabbage.

Lederberg: I think you should be quite cautious about exposing people to a great deal of jute pulp until tests have been carried out.

Price: In Malaya the Chinese girls eat certain pineapple shoots as a birth control measure.

Pirie: Are they effective?

Price: They are said to be!

Wright: There are tremendous potentialities in the oceans which we have not mentioned so far. Only about one-tenth of the world's animal protein and one-hundredth of the world's total food supplies are derived from this source. There is no doubt that the potentialities for catching fish, and for fish culture inland, in tanks, are both enormous and economic. The latter is already being developed on a very considerable scale.

Hoagland: There is one source that has not been tapped in the Antarctic, namely, squill, the shrimps that form the favourite food of the baleen whales. They are said to offer a yield of animal protein per unit area of ocean something like several times the yield of the best land grazing areas. They are exceedingly plentiful but as far as I know no one has made any serious attempt to harvest them.

Clark: An attempt was once made in Australia. The distances are such that it was found uneconomic, at the present price of proteins, but when they go up this may change. The FAO report on *Fish Farming and Inland Fishery Management* (1954) and some work from Nigeria (see Pedler, *Economic Geography of West Africa*) suggest a gross yield from fish in ponds up to 2 tons per hectare per year. The Danish oceanographic research ship found a rate of photosynthesis in some parts of the oceans of about 5 grams per square metre per day, which is comparable with ordinary farm land. This is in regions where the upwelling

currents make the ocean rich in phosphates. If we are looking right into the future, our descendants may be able to fertilize the ocean as well as the soil: with inland fisheries this is being done now.

Hoagland: There has been controversy recently in the United States over a technique to make a protein-rich concentrate by grinding up entire fish—scales, head, intestines, everything. These are waste fish not used by man for his table. This protein preparation has been condemned by the Pure Food and Drug Act as "filthy" food. Thus labelled it cannot be sold for human consumption. It would be much too expensive if they tried to clean the fish and just use the muscle. This looks like a good way to obtain quantities of animal protein.

Coon: Within the last week or so that decision has been reversed and they have started to make whole-fish protein in Gloucester, Massachusetts.

Klein: I think we should all once in our life read Malthus' *Essay on the Principle of Population.* It is not altogether a pleasant book but plenty of the things we are discussing here today are actually to be found there already, in the successive, numerous and revised editions from 1798 onwards, and we should also remember that Darwin derived his own inspiration from Malthus.

I enjoyed Professor Brock's paper immensely, because, being myself a biologist in a medical school, I feel we have common interests in all that he has shown. We should be particularly careful about what Brock called additives, especially about the anti-oxidative substances which are added to things we eat and drink, and particularly the group of enzyme inhibitors (monobromoacetic acid or monoiodoacetic acid).

In my own laboratory Karli has performed experiments on rabbits which show that extremely minute doses of monoiodoacetic acid destroy the retina of the eye, and spermatogenesis suffers immediately too. Thus we are all getting in our daily food very small amounts of substances potentially dangerous to the condensed nuclei of cells. The whole group of enzyme inhibitors is to be included in this category. There is also

another group which Brock did well to mention that includes aluminium. Experimentally, when you give aluminium salts to mice you completely arrest the ovarian cycle. Some years ago there was anxiety about whether enough aluminium salts might remain in some baking powders to produce effects on peptic ulcers or even perhaps on ovogenesis and spermatogenesis.

Clark: Do you object to aluminium kitchen implements?

Klein: In man nothing definite has been shown, but in experimental animals such additives are dangerous.

Glikson: I should like to make a general remark with reference to Colin Clark's paper. His plan for a world population of 45,000 million people seems to be based on a calculation of a person's physical minimum requirements, and the earth's resources of cultivable land. I cannot discuss the accuracy of this calculation, but I think a distinction must be drawn between a level of bare survival and the level of living a full life. Even if the calculation were correct, the 45,000 million would be just able to survive.

Clark: No. They could live at the physiological *maximum*—ten times as many could survive at the minimum level.

Glikson: "Survival" is not a human condition which promises a balanced existence or peace for any length of time; this notion disregards the need of land, space and commodities for the creation of any values other than basic calories and a few vitamins. Space must be available for the great variety of human requirements of land use and ways of living. Some land "surplus" appears essential for the establishment of a satisfactory community life.

In considering possible future population densities, I would have expected to hear of research, not about minimum food requirements, but about the optimum diets to be provided as a basis for happier and healthier human lives. Obviously such research would have to be done on a regional basis taking account of all the varying environmental conditions and the physical and psychological human requirements of each region.

Control of Reproduction in Mammals

GREGORY PINCUS

The magnitude of the population explosion has been recognized by demographers, economists and sociologists and with it the need to develop new methods of fertility control[1]. Methods in common use in Western countries have been found to be impracticable or unacceptable in many areas of the world. Furthermore, the use of what are principally barriers to sperm access to, or movement in, the female reproductive tract is, even under controlled conditions, accompanied by some risk of conception (see Table III below), and more "fool-proof" methods of contraception are therefore desirable.

When we consider the delicately balanced set of sequential processes involved in mammalian reproduction, it is clear that there are many possibilities for control by immunological, hormonal or other means of manipulation. I have discussed a number of these in detail in a forthcoming book on *The Control of Fertility*[2]. As the result of research which Dr. Chang and I initiated with animal experimental work some ten years ago, a highly effective method of oral contracepton has been developed which is now in increasingly wide use. It is based upon our knowledge of the processes which effect the liberation of the mammalian egg (the ovum) in the process of ovulation.

The development of the mammalian egg begins with the formation of the germ cells in the embryonic gonad. According to the best evidence at present available, the ovary at birth contains all the oöcytes (primitive ova) destined to last for the female's reproductive life. The slow maturation of the ovaries before puberty involves chiefly the development of the follicles surrounding the egg, until at puberty ovulation is initiated: an egg is released by rupture of a ripe follicle. Thereafter ovulation

occurs cyclically and the periodic production of eggs is halted only by pregnancy or, in animals, by anoestrus. The ovulated egg is normally fertilized in the Fallopian tube, travels through the lower portion of the tube for some days, enters the uterus, and eventually implants in the endometrium (lining of the uterus) where its growth into a foetus takes place. I should like to consider experimental data concerned with: (1) The control of ovulation in animals and some applications to the human and (2) some aspects of the physiology of ovum development preceding implantation.

CONTROL OF OVULATION

A general concept of ovulation-controlling mechanisms may be framed as follows. The hypothalamus (an area at the base of the brain) produces a substance, known as a neurohumour, which enters the anterior lobe of the pituitary gland and acts upon it to stimulate the secretion into the blood of a hormone (gonadotropin) generally called luteinizing hormone (LH). It is LH which enters the ovary from the blood to stimulate the pre-ovulatory swelling and final rupture of the follicle. The corpus luteum formed from the ruptured follicle produces large amounts of (steroidal) progestational hormone exemplified by progesterone. Progesterone in turn acts upon the hypothalamus to inhibit the production of the LH-stimulating neurohumour. Thus, since progesterone is secreted in large amount during pregnancy, ovulation cannot occur during that critical period. There are a number of variations to this general scheme but it is basic to the ovulation process in all mammals.

It is clear from the foregoing that there are four loci essential to ovulation and that each of these is open to experimental attack. These loci are: (1) The hypothalamus, essentially a nervous structure; (2) the anterior pituitary, essentially a secretory gland; (3) the general blood circulation as a carrier of gonadotropin (LH); and (4) the ovarian follicle. Experimental studies of ovulation control have largely centred on control of hypothalamic activity leading to ovulation. This is because it was known that progesterone and also a number

of drugs will inhibit the production of ovulatory neurohumour by the hypothalamus. These drugs include barbiturates, certain tranquillizers, morphine and ether. The doses necessary for such inhibition appear to be rather high and this is probably why their experimental study in the human has not been carried on to any extent. The situation is quite different with progesterone, where we can clearly see ovulation inhibition at physiological doses.

Experimental work with loci other than the hypothalamus has been much more limited. Thus no substances have been found which have a direct stimulating or inhibiting effect on the pituitary, i.e. which do not act via the hypothalamus.

Several means of affecting LH in the circulating blood have been investigated. These include extracts from plants (*Lithospermum ruderale* and *Lycopus virginicus*) and from pituitary glands, foetal blood serum and human urine. None of these agents are chemically defined, and the nature of their action is often dubious: the plant extracts are postulated as acting by destroying gonadotropin by enzyme action, and the animal substances as acting as competitive inhibitors to gonadotropin. Perhaps the most promising inactivator at present is LH antibody, which is prepared by making an antiserum to LH. It inactivates LH in the blood by combining with it to produce an inactive compound. The fact that the LH antibodies of some animal species are able to inactivate the LH of other species implies that it might be possible to use animal antibodies in man; however, very much remains to be learned about long-range effects, the possibility of isoimmunity, sensitivity reactions and so on.

Concerning the fourth locus—the ovarian follicle itself—again there is only limited experimental work to consider. Curiously, the most effective drug which directly inhibits follicle rupture is reserpine, a substance which also inhibits the hypothalamus. Certain steroids (i.e. substances with the same chemical skeleton as the sex hormones) are active also, but again at very high doses. It should be emphasized, however, that animal work in this area is still at an early stage and it may be predicted that interesting discoveries will come in the future.

Undoubtedly the most active experimental work has been with steroidal inhibitors of ovulation acting via the hypothalamus. Our re-investigation of the effect of progesterone in inhibiting ovulation in the rabbit was followed by the discovery of certain synthetic steroids, known as 19-norsteroids, which show progesterone-like activity when taken orally. Subsequently many studies of these and related anti-gonadotropic steroids have been carried out on animals. In a study of several hundred steroids in the rabbit, we have to date found 67 active compounds, and with a different series of steroids Kincl and Dorfman have found approximately 50 active compounds, but only a few of these compounds exhibited sufficient activity to be of possible practical importance.

The comparative potency of these compounds as ovulation inhibitors in women has so far not been examined in detail, but we have had some evidence that substances shown in the rabbit to be more active when administered orally than by injection are excellent oral ovulation inhibitors in women[3]. In women, the compound most extensively studied has been norethynodrel. It is ordinarily administered in combination with an oestrogen in a preparation called Enovid. This combination effects adequate control of the endometrial blood vessels, thus avoiding bleeding during medication. On withdrawal of the medication, a menstrual flow follows in one to several days. Thus by employing a medication regimen requiring the taking of a single tablet each day for 20 days beginning on the fifth day of the menstrual cycle, an average cycle length of 28 days has been attained. Furthermore, with faithful following of this regimen, a remarkable succession of regular menstrual cycles may be attained year after year. In a five-year period of study of volunteer subjects taking Enovid, it was found that, although the first few cycles might be short, with premature bleeding, the endometrium soon accommodated to the medication, and thereafter short cycles with premature bleeding were relatively infrequent. Such bleeding occurred more frequently at low dosages of Enovid (2·5 mg. per day). When the dosage of Enovid is 5 or 10 mg. per day, the frequency

of such short cycles is less than that observed in normally-menstruating women, i.e., 3·2 per cent for 10 mg., 4·9 per cent for 5 mg., and 10·4 per cent in the non-medicated, normal menstrual cycles.

The volunteers in this project have employed this method of ovulation inhibition for purposes of contraception. The record from April, 1956 to December, 1961 of conceptions at the various dosages we have used is given in Table I[4]. The conception rate is remarkably low, and control at the lowest dosage

Table I

FERTILITY IN PATIENTS TAKING ENOVID

	Daily dosage of Enovid		
	10 *mg.*	5 *mg.*	2·5 *mg.*
Number of pregnancies	22	15	3
Years of medication	789·3	1,579·1	217·8
Pregnancy rate per 100 woman years	2·8	0·95	1·4

employed (2·5 mg./day) is just as effective as at the highest dosage (10 mg./day). We have several times pointed out that with faithful following of the medication regimen, contraceptive efficiency is practically 100 per cent. This is illustrated in Table II, which compares the conception rates for women

Table II

FERTILITY IN PATIENTS TAKING ENOVID

Number of tablets missed	*Number of pregnancies*	*Years of medication*	*Pregnancy rate per 100 woman years*
0	4	2,343·4	0·17
1–5	16	193·2	8·3
6–19	20	49·6	40·3
All cycles	40	2,586·2	1·5
Controls	124	59·0	210·0

allegedly taking a pill every day during the 20 days, for those missing a few pills and for those missing more than five pills.

It is obvious that faithful tablet-taking gives practically complete contraception. But even when some tablets are missed, a clear reduction in fertility occurs, for among these women when no contraceptive is being used the conception rate is 210 for 100 "woman years" of exposure. Dr. Venning has compared the conception rates reported for Enovid and for various other methods of contraception. This comparison is shown in Table III; it is obvious that Enovid taken by mouth offers by far the most efficient method of conception control.

In conducting these trials with Enovid, we have maintained a close follow-up of all of the volunteer subjects. In addition to regular monthly visits with a nurse or social worker, we have conducted annual examinations of most of the women[3,4]. I should like here to present data on certain aspects of the use of the ovulation-inhibiting, menstruation-regulating regimen. I have already indicated that a succession of quite regular menstrual cycles is usual in women taking Enovid. In addition, we have questioned patients from time to time concerning the nature of the menstrual flow. Their replies indicate that, compared with the premedication flow, menstruation appears to be ordinarily unchanged or somewhat lighter, but seldom heavier. This ability of the drug to reduce menstrual flow has led to its therapeutic use in many conditions involving excessive menstrual flow.

In order to study the effect of Enovid on lactation, we have been giving the drug to a group of women three to six weeks after the birth of a baby. At the highest dose (20 mg. a day) a substantial majority noted a reduction in milk production, but at the lowest dose (2·5 mg. a day—which is just as effective in contraception) the majority noted no change, and those finding lactation less just about equalled those finding it increased.

Our patients have kept track of body weight changes. There is a suggestion that a significant proportion of women taking the 10 mg. dose tend to gain weight, but this is not evident in the lower dosage groups, and over-all reports of weight gain tend to balance those of weight loss.

Table III

EFFECTIVENESS OF DIFFERENT METHODS OF CONCEPTION CONTROL, TAKEN FROM SEVEN PUBLISHED REPORTS*

Method	*Indianapolis*	*Belaval et al*	*Morgan and Beebe*	*Tietze*	*Princeton*	*Dubrow and Kuder*	*Average pregnancy rate per 100 woman years*
Douche	21	—	—	36	41	—	31
Safe period	—	—	—	14	38	—	24
Jelly alone	—	28	—	4–38	—	7·6–8	20
Withdrawal	10	—	—	12–38	17	—	18
Condom	7	—	22	6–19	14	—	14
Diaphragm (with or without jelly)	4	30	9	6–13	14	8·9–9·7	12
Enovid	—	—	—	—	—	—	1·2†

* Table taken from letter to British Medical Journal (p. 899, **2**, 1961) by G. R. Venning.

† Over-all pregnancy rate based on 578 woman years (approximately 7,000 cycles) including cycles in which tablets have been missed.

The women were also questioned about changes in libido. About 80 per cent report no change, 5 per cent to 8 per cent an increase and 13 per cent to 18 per cent a decrease. The extent to which modesty governs these answers is, of course, imponderable, but certainly no drastic change is indicated.

In recent years, several other ovulation-inhibiting steroids have been studied in similar field trials. These have been chiefly 19-norsteroids used in combination with an oestrogen. Among the objectives of research on other compounds is the discovery of substances effective in even lower doses than those now available in order to provide a relatively inexpensive medication. However, in order to obtain adequate menstrual control, such compounds must be potent regulators of endometrial function as well as inhibitors of ovulation.

We have in progress a study of a substance called ethynodiol diacetate (ED). Because of its good ovulation-inhibiting activity in test animals, we initiated our study in women with 2 mg. tablets of ED plus 0·1 mg. of the oestrogen we have used with all our progestins. In over 100 women who have used this medication for periods of up to 16 months, we observed the same general phenomena seen with Enovid: initially 16 per cent showing "reactions" and 6 per cent showing premature bleeding, both of which have become minimal by the fourth cycle of medication. Thus far in nearly 100 "exposure years", no conceptions have occurred among these women, probably because of their realization of the need for regularity in tablet taking.

The "reactions" reported by these volunteers are occasional headache or dizziness, or nausea or vomiting. We have data indicating a large psychogenic element in their occurrence. Most of the subjects in these ED experiments were questioned prior to their entry into the project concerning the occurrence of such symptoms during their regular menstrual cycles. Of the 122 patients responding to this questioning, 48 reported having had similar symptoms and 74 said that they had no such symptoms. More than half (58 per cent) of the women studied had such symptoms before medication but were "cured" during medication. On the other hand, 39 per cent of these women

allegedly had no such symptoms previously but had them "induced" by the medication. Therefore these occurrences appear to be random events and exhibit no consistent relationship to medication.

After the initial four to six months of use of this drug by a first group of volunteers, we questioned them about weight changes, breast size, menstrual flow, pain during menstruation, libido and frequency of coitus. Except for some tendency, not unexpected, to a decrease of menstrual flow, no significant changes were noted, the decreases tending to balance increases.

It is clear from the foregoing that effective inhibition of ovulation by oral medication has been definitely accomplished in the human being. Rice-Wray and Goldzieher have recently reported on comparative studies with 2,432 women observed in 22,948 treatment cycles. Five progestin-oestrogen preparations were used with complete effectiveness upon proper use of the regimen in which tablets were taken daily from the 5th to the 25th day of the menstrual cycle. Regularly achieved ovulation control may therefore be taken as a fact. Indeed, contraceptive research projects with steroidal ovulation inhibitors have been conducted throughout the United States, in certain European countries, in Japan, Ceylon, Singapore, Hong Kong and India, with remarkably similar data coming from each.

CONTROL OF THE DEVELOPMENT OF THE FERTILIZED OVUM

Our studies on the control of the development of the fertilized mammalian egg originated over 20 years ago when Dr. N. T. Werthessen and I followed up an original observation by Dr. George W. Corner. Corner found that in rabbits whose ovaries were removed shortly after fertilization the egg enters the uterus at the normal time but fails to grow to normal size or to implant. However, with the administration of an adequate dose of progestin to such animals both normal ovum growth and implantation may be restored. Dr. Werthessen and I developed this ovum response as part of a quantitative assay for progesterone. We found, furthermore, that oestrogens administered with the progesterone could inhibit the growth of the ovum and/or the

uterine response to the progestin. Recently, Dr. Miyake, Miss Merrill, Miss Longo and I took up this question again and developed another assay method for progesterone involving measurement of an enzyme in the endometrium. Using this enzyme method we were able to measure the antagonistic, or antiprogestational, effect of the oestrogens, and were thus able to examine a large number of steroids as possible antiprogestins.

We found a limited number of significantly active compounds[5]. These fell into two categories: (1) derivatives or close chemical relatives of the steroidal oestrogens and (2) certain other steroids without oestrogenic activity. The first group appear to act as physiological antagonists and the second as competitive antagonists. Among the compounds of the second group, several appear to have only this progesterone-inhibiting effect and no other hormonal activity, in contrast to the oestrogen derivatives, which possess the numerous functions associated with oestrogen activity.

On the assumption that antiprogestins should act to inhibit ovum growth and implantation, Dr. U. Banik and I have examined the effects of a number of these compounds administered to rats and mice carrying fertilized ova. Females were caged with males overnight and examined the next morning for the presence of vaginal plugs and sperm to ensure that copulation had taken place. Administration of the antiprogestins was begun 24 hours later (called day 1 of pregnancy) and then on two subsequent days. Most of the compounds tested did indeed inhibit implantation in both rats and mice. Some of the others appeared to be effective in one species only, whereas some failed to inhibit implantation despite administration at comparable dose levels. In addition, it should be noted that antiprogestational activity in the rabbit is not paralleled by implantation inhibition in rats and mice. We have observed too that among the active compounds doses that are less than 100 per cent effective in preventing implantation may still significantly reduce the number of uterine implantations.

Dr. Banik and I thought that since implantation occurs by the eighth day its inhibition could be more easily accomplished

by administration of the antiprogestin later rather than earlier in the pre-implantation period. To our surprise, administration on day 1 alone was uniformly effective whereas administration on day 3 alone was either ineffective or very much less effective. Indeed, these same antiprogestins administered on day 8 or later were practically ineffective in causing death or resorption of the embryo. We have, therefore, a group of compounds which will uniformly prevent the free ovum from becoming implanted provided that they are administered on the day following mating.

This unexpected effect of compounds originally chosen because of antiprogestational activity on the endometrium raises many questions concerning the factors and processes involved in free ovum development. Thus normal-appearing blastocysts are recovered from the uteri of animals receiving sterilizing doses of antiprogestins. Why do they fail to implant? A large proportion of sterile women apparently ovulate normally but fail to have implantations. Is it possible that certain steroids produced by the ovaries or adrenal glands of these women act the way our implantation-inhibiting steroids do? How will these compounds affect human reproductive processes? It is, I believe, clear that many interesting problems remain for study.

CONCLUSIONS

I have attempted to present here the highlights and to dwell briefly on some implications of investigations into aspects of the life history of mammalian eggs. To me it is a most fascinating field for research, perhaps because we are indeed just at the forefront of an era where these and numerous other mysteries of reproduction will no longer be mysteries. But it is clear even now that exceptionally effective methods of fertility control are at hand and that others are in the offing. The most promising are those concerned with inhibition of the development of the ovum, and this is perhaps auspicious since it is women who must bear the major burdens of reproduction and who, indeed, have been the major seekers of relief from these burdens.

In presenting the history of certain special efforts in fertility control, I have attempted to indicate how facts derived from

laboratory research have led to practical application. Numerous similar developments may be confidently predicted and scientific methods for fertility control will be multiplied. Man's effective control of his own reproductive capacity is inescapable.

The Sex-Ratio in Human Populations

A. S. PARKES

THE study of human biology is handicapped in many ways, but it has some advantages for quantitative work because human beings are produced in huge numbers compared with any experimental animal and are comparatively well documented. This advantage is well shown in the study of the sex-ratio. The proportions in which the sexes occur has attracted attention from early times and it is a matter of general interest because the simple facts and their more obvious social implications can be understood by anybody.

The best known fact is that the ratio of the two sexes at birth is not quite equality, as would be expected on the chromosome basis of sex determination, but fluctuates around 105 males per 100 females. Over millions of births, this slight excess of males cannot be due to chance and we must consider its significance. In England and Wales at the present time there are about 106 males per 100 females at birth. The proportion has not always been as high as this; it has been increasing irregularly for some 70 years. Fig. 1 shows the sex-ratio of births by 10- or 5-year periods from 1841 up to the present time. The decrease in the number of males at birth during the first 30 years of this period is not easy to understand; possibly registration was incomplete. For the next 40 years the ratio hovered below 104 males per 100 females and then coincident with World War I rose rapidly to about 105. A subsequent decrease was followed by another sharp rise reaching a peak coincident with World War II. On the huge numbers concerned these changes must mean that something happens from time to time to the sex-ratio of live births, and that the general level for this century is higher than the level for last century.

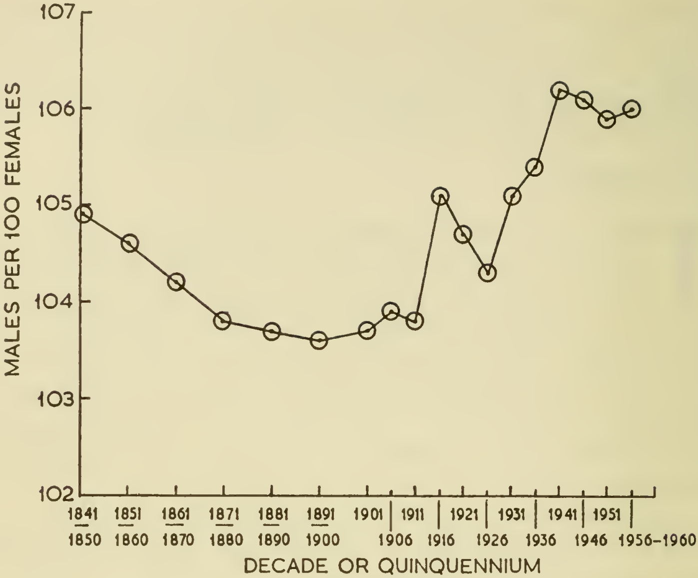


Fig. 1. Sex-ratio for live births in England and Wales, 1841–1960.

The ratio, however, changes in another way. In years gone by, the excess of males at birth disappeared by the age of 5 years, because of the differential mortality of males over this period, and thereafter females were in excess. By the turn of the century, mortality had decreased and the ratio hovered about numerical equality between the sexes up to the age group 15–19 years, and then owing to differential mortality and emigration the ratio fell sharply to below 90 males per 100 females in the 25–29 age group. At the present time, with the further decrease in child mortality, the excess of males found at birth is being preserved much longer, up to the age group 25–29 years.

The effect of differential mortality on the sex-ratio continues throughout the life cycle (Fig. 2). Thus, even now, females exceed males from the age group 35–39 onwards and the decrease in the relative number of males becomes very sharp after age 55. It is in fact sharper at the present time than it was in

1901. It seems, therefore, that the progress of medical science has preserved the excess of males at birth well into adult life, but that by contrast, in middle and old age, it has done more for women than for men.

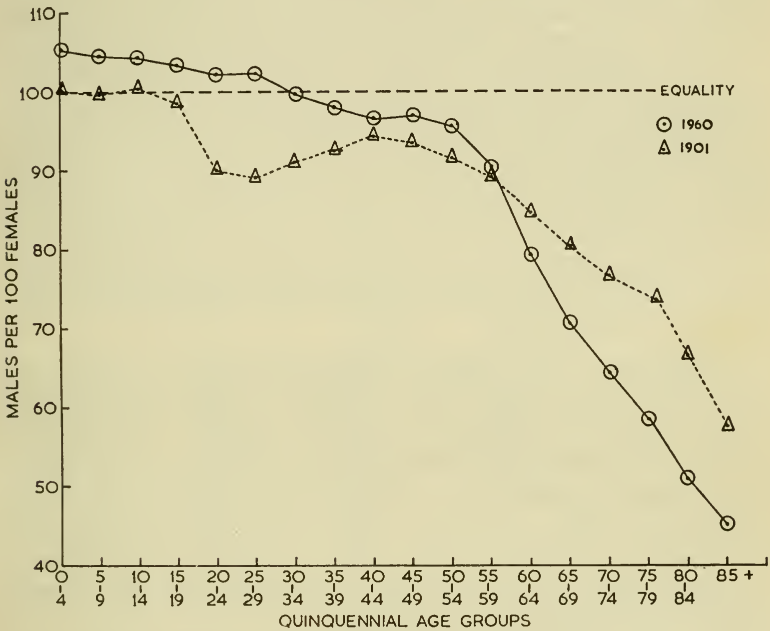


Fig. 2. Sex-ratio according to age (England and Wales).

The sex-ratio among adults at successive stages of the life-cycle is, therefore, much affected by differential postnatal mortality. We must now ask whether the sex-ratio at birth is influenced by differential prenatal mortality and if so, whether this fact has any bearing on fluctuations in the sex-ratio at this time. Unfortunately, very little is known about the sex incidence of prenatal mortality or of the sex-ratio of living foetuses at various stages of pregnancy, either in man or animals, but some facts are available. Firstly, there was until quite recently a large excess of males among stillbirths. This fact may be taken

as an indication of the lesser viability of the male foetus, a conclusion which is supported by the fact that observations on the sex incidence of abortion have usually shown a large excess of males. It might be supposed, therefore, that the earlier in pregnancy, the higher the proportion of males among live foetuses. This conclusion, however, has not always been borne out by examination of the sex-ratio of live human foetuses removed for therapeutic purposes. It is to be hoped that conclusive figures on this point will be forthcoming from the mass abortion programmes being carried out in Japan and other places. Evidence from mammals, however, has in some cases shown a steadily decreasing ratio of males during pregnancy. The domestic pig is very suitable for studies of this kind and Crew estimated the sex-ratio at conception in pigs at about 150. Recent work on the golden hamster also suggests a very high sex-ratio at conception.

Another way of looking at this problem is to consider the sex-ratio of living births under conditions where prenatal mortality is known to be high, as with older mothers. The sex-ratio of live births during a recent quinquennium was much higher with younger mothers than with older ones. This fact probably explains the effect of the two world wars, which substantially lowered the age of marriage, on the sex-ratio. In doing so, it explains neatly the old idea that nature increases the sex-ratio after wars to replace the lost males.

The extent to which the prenatal sex-ratio is affected by differential mortality will of course depend on the amount of mortality as well as its sex incidence. Overt abortions are said to amount to about 20 per cent of all pregnancies, but loss in the early stages is probably much greater. Total prenatal mortality is therefore heavy and almost certainly falls differentially on males. It is thus very likely that there is a large excess of males at conception; estimates of the sex-ratio in man at this time vary between 120 and 150.

This probability of a large excess of males at conception raises some interesting social and biological problems. First, as prenatal and postnatal mortality decreases still further, the excess

of males will persist later and later. If and when the sex-ratio at conception, or anything like it, is carried through to marriageable age, there will certainly be remarkable social repercussions. Even now, women are beginning to have the scarcity value previously held by men and it is to be hoped that competition among men for females may have the effect of making them more colourful. But the transformation of men into human peacocks, however striking, would be only one effect.

Table I shows the situation in England and Wales in 1960 resulting from a sex-ratio at birth between 104 and 106. This table gives the actual excess of males in thousands up to the age of 29 and the excess of females thereafter. Obviously, at the

Table I

EXCESS OF MALES OR FEMALES AT MARRIAGEABLE AGE

1960

THOUSANDS

Age groups	*Males*	*Females*	*Excess males*	*Excess females*
15–19	1560	1509	51	—
20–24	1482	1451	31	—
25–29	1446	1414	32	—
30–34	1491	1497	—	6
35–39	1646	1680	—	34
40–44	1451	1499	—	48

present time, the excess of males at early marriageable age is not sufficient to bring social pressures which might result in the legal and religious recognition of polyandry. What then can happen, now and when the excess of males increases and persists still longer? The simplest solution would be for everyone to wait, before getting married, until enough males had died to restore numerical equality between the sexes, at present at about age 30 years. Another possibility is that the female vacuum at early marriageable age would draw in females from other countries, possibly from the Common Market. This is not likely to happen because the tendencies discussed are found in most countries; we are in fact heading for a world shortage of marriageable females. Another possibility is that the surplus

males in the lower age groups would pair off with the surplus females in the higher age groups, many of whom, of course, must be widows. This again is not likely to happen on any large scale. What is going to happen, according to the demographers, is that the excess males will find their females not by going after widows, but by robbing younger age groups of females. This, of course, would set up a chain reaction so that males would necessarily seek younger and younger females. The existing situation is only a foretaste of what may come if and when a large excess of males appears at marriageable age, and the logical conclusion of the expert view is that oldish men will be bespeaking newly born females.

We must now consider the biological aspects and implications of the probability that there is a large excess of males at conception. First, how is this explicable in the light of the chromosome mechanism of sex determination, which implies the conception of equal numbers of males and females? There are two obvious possibilities. One is that in spite of the chromosome mechanism, the actual production of normal functional spermatozoa is not in the ratio of 1:1, and the other is that the Y male-producing spermatozoa have some advantage over the X female-producing spermatozoa in the female tract, so that a larger number reach the site of fertilization. One or other of these possible factors operates to produce the male excess at conception unless there is some less obvious cause.

The second point of biological interest is the evolutionary significance of the high ratio at conception. It might be said, perhaps, to have the purpose of allowing for subsequent male loss and so maintaining the ratio among adults at 1:1. But what, in fact, is the evolutionary value to mammals of such a ratio? Surely numerical equality between the sexes is a hang-over from those lower vertebrates in which the reproductive potential of the two sexes was nearly equal and in which therefore equal numbers of the sexes were required for maximum reproductivity. On this view, the 1:1 ratio in mammals is something of a biological anachronism. With the very large difference in the reproductive potential of the two sexes, a sex-ratio of

1:1, from the point of view of maximum reproductivity, is simply a waste of male biomass. Biologically, it can be argued that there are something like a million tons of unnecessary men in this country alone. The record production of a woman is said to be something over 50 children, a total much increased by the birth of twins and triplets which could not normally be relied on. A fertile man, on the other hand, could easily father 500 children, or considerably more if he got himself properly organized. Possibly, therefore, in man a ratio of one male to ten females would ensure maximum reproductivity in relation to biomass and a ratio of this kind might therefore expect to have a substantial survival value.

This thought raises two further queries: one social, one biological. First, what social changes and ultimate social organization would be brought about in man by a permanent sex-ratio of 10 males per 100 females? Obviously universal polygamy would be inevitable and the moral and legal codes relating to sexuality would change accordingly. Monogamy rather than polygamy would become the social crime, and men, like drone bees, would be expected to do little except reproduce their kind. Women would do the work as well as bear the children, as in fact happens at present in many primitive peoples, and the complications of surtax would be unimaginable.

All this may be good extrapolation, but in fact we are stuck with the chromosome mechanism. What then can be done about controlling the sex-ratio to individual wishes or national needs? It may be that, sometime in the future, biological science will solve the problem of breeding XX female-producing males or obtaining parthenogenetic humans which, according to theory, would inevitably be female. More likely, it may become possible to accentuate the factors, if any, which affect the ratio of normal mature spermatozoa produced by the testis. But the only procedure at present even remotely in sight is the *in vitro* separation of X- and Y-spermatozoa, combined with artificial insemination. As this would not necessarily involve donor insemination, it might be socially acceptable. Claims to have separated animal or human spermatozoa into two groups by

electrophoresis or differential centrifugation have been made. In the case of rabbits and cattle, there have been claims, supported by breeding experiments, that the two groups separated were in fact X- and Y-spermatozoa. All this work, however, is in serious need of repetition and confirmation on a large scale. Immunological methods are also being investigated for the possible separation or differential destruction of one or other type of spermatozoa.

Assuming that the separation of X- and Y-spermatozoa will be effected one day, and I have no doubt it will, what are the chances of preserving the separated gametes for future use as required? At present, the only practicable approach to the long-term preservation of mammalian cells is so to reduce the ambient temperature that the biochemical and biophysical processes of life are attenuated sufficiently to cause the cell or tissue to pass into a state of suspended animation. Up to about 12 years ago, such a method had been effective with only one or two types of normal vertebrate cells, but it was then discovered that the otherwise fatal effects on cells of freezing and thawing could in many cases be very largely avoided by the use of protective substances, of which glycerol is the best known. This particular technique was first evolved on the spermatozoa of domestic fowl, not on mammalian cells, but it was very quickly adapted to the spermatozoa of the bull because of the economic importance of efficient use of bull semen in artificial insemination centres. In man, of course, there have been attempts over this period, and long before, to preserve human spermatozoa at low temperatures. Some success has been achieved: there have been reports in America of one or two children being produced as a result of artificial insemination with preserved spermatozoa. The whole subject, however, is at a very elementary stage; it is nothing like so far developed for man as for farm animals, especially the bull, for which posthumous paternity is now possible many years after death. Obviously a great deal more work will have to be done before the long-term preservation of human spermatozoa, whether or not separated into X- and Y-types, becomes practicable. There

is little doubt, however, in my mind, that an intensive drive, if it were thought desirable, would produce this result in a short time.

There is one final point here which is of some importance, I think, in connexion with our present discussions ; so far as work on animals is concerned, exposure to and preservation at low temperatures may or may not kill any particular spermatozoon, but it does not damage the genetic properties of those still able to effect fertilization. It seems that the damage caused to spermatozoa by low temperatures, which can be overcome to varying degrees by special methods, is first to their vegetative functions, rather than their genetic material, so that if a spermatozoon preserved at low temperature is able to effect fertilization, it will, according to experience with animals, produce normal young.

By contrast with the male gamete, the preservation of ova, whether fertilized or not, has hardly been investigated as yet, and so far, even in mammals, I do not think that either fertilized or unfertilized eggs have been preserved for any significant length of time. Moreover, techniques are much complicated by the fact that as yet, even in experimental mammals, ova can be obtained only by means of surgery, and the same applies of course to the transference of eggs or their return after *in vitro* treatment. However, all these problems will be solved one day or other, and the transference of fertilized eggs of the required sex will be possible in man in the course of time.

Among the many sociological queries arising from such prospects is this: if the sex of the projected child could be chosen by the parent, which sex would be chosen more frequently? With the present social set-up, it is doubtful whether the overall ratio would be much affected, as witness the common anxiety to have a family nicely balanced between boys and girls. In fact, we may conclude that even if and when sex predetermination becomes possible, so far as the sex-ratio is concerned the future of man will be about the same as his past.

DISCUSSION

Klein: The ovulation-inhibiting compounds that Dr. Pincus has talked about are mainly progestins. The very first function that was ascribed to the corpus luteum (which produces the natural progestins) was the inhibition of ovulation. This was suggested by Prenant, and by Beard as long ago as 1898.

Professor Parkes has told us that we are extrapolationists. This is a very good idea, but I am afraid that within it lies the main danger of all we are to discuss here. Within what limits can results obtained on animals be transferred to human beings? This is a question which can be considered on two levels: first, on the technical and biological level, and then on what we should call the normative level. We ought to be very careful about the distinction between what we call descriptive sciences and normative sciences. I feel that this distinction is not being made. Dr. Pincus said that it is desirable for us to control reproduction—not only in number, but perhaps also in quality. The word "desirable" shows that there is a definite human plan. From the technical point of view there is not much difficulty now in controlling reproduction. As Dr. Pincus has shown, there are a number of substances which can interfere with reproduction, in either the male or the female, and Dr. Parkes has indicated that it will soon be possible to control the ratio of the sexes. But is it desirable? And, if so, how can this be done in a human way?

I should like to add here a brief point from my own experience. Sometimes outside the professional field something happens in the life of a man which completely changes his way of thinking, and such a thing happened to me. I spent a whole year in the worst Nazi concentration camp, Auschwitz

Stammlager, where there was an experimental station run by an endocrinologist named Clauberg. I was told when I arrived in the camp never to disclose that I was an endocrinologist, otherwise I believe I would have been put into Clauberg's team. As everybody now knows, huge experiments were performed there on the sterilization of both men and women. Once you have seen with your own eyes where those problems can lead, you are always very cautious, even when you hear about the very beginnings of this type of experiment.

Even today there is still a large gap between what has been done in the best experimental series on animals and what has been done or might be done on human beings in view of the future. This brings us to the most general question of all, prognostication. What we are doing here is making prognostications for the human community. And a question which will be raised many times in our discussions is, what is more important—the individual or the community? If you answer "the individual", you take a different path in the present and in the future, from the one you would take if your answer is "the community".

Brock: I should like to hear something from Dr. Pincus about the political acceptability of chemical contraception. It seems to me that in underdeveloped countries the political objections to reduction of population are possibly as important as any religious objection.

Pincus: Members of the Eugenics Society in Greece, who asked me to lecture on this subject there, were most interested, but thought this work irrelevant to the problems in Greece, where they felt the population should increase to withstand the encroachment of its Communist neighbours. I am sure that everyone here has heard similar comments. In India, on the contrary, it is recognized that birth control is important for the well-being both of the family and of the community.

Let me emphasize that in India and in the other countries of the Far East that I have visited, only voluntary control has been envisaged. Voluntary control can only be exercised by adequate education and motivation; and the problem of adequacy of

motivation in these countries is still unanswered. I can cite two experimental studies as examples, although they may not apply to larger groups. The first of these was conducted in Bombay with one of the conventional contraceptives, an intravaginal foam tablet. This was done under the best possible auspices by a group of very able physicians who went into the slums of Bombay and secured volunteers to use these foam tablets. At the end of one year only 12 per cent of the women who were originally enlisted in the project remained; at the end of two years practically none. This method was rejected on various grounds—but nonetheless rejected. In contrast, our experience with oral contraception in Puerto Rico has been almost the reverse: there is a drop-off in numbers, but it is the lowest for any type of contraceptive that has ever been studied. Haiti unfortunately gives us no opportunity for comparison, because they never had any previous contraceptive study, or even very much available in the way of contraceptives. So we are in a state of uncertainty about motivation, or about political opposition. In Haiti our work has been conducted as a private project, without government opposition. In Greece such measures would probably be opposed. In India they would be encouraged.

Trowell: In underdeveloped countries from a quarter to a half of the children die in childhood, so that parents desire to have as many as possible. The first step in spreading the idea of family planning is to reduce infantile mortality that is due to a combination of disease and malnutrition.

Klein: We have been talking about underdeveloped countries, but what is the situation now in more civilized countries where contraception was prohibited but where the law will now perhaps be changing slowly? Have you got any information on the reaction of European countries to such plans? Do you think this question should be left to people who are working on demographic inquiries or to medical biologists specializing in reproductive physiology?

Pincus: The tide of public opinion appears to be changing in many countries, as it has in Haiti, for example. I have had

no experience in Europe. I only know that these drugs are sold in the countries where contraception is accepted.

Wright: I gather, Dr. Pincus, that the tablet method is better than mechanical means so far as "accidents" are concerned, but you did give examples where women forgot to take tablets and conception occurred. Has the possibility of incorporation in some other form, such as food, been considered? I am thinking particularly of condiments such as salt—something that would normally be used in the household but that could be easily differentiated for particular individuals within the household, and that would not normally be forgotten as tablets can so easily be.

Brain: Isn't part of the problem the fact that at present something requires to be taken daily for a long period, and it is important to know whether it will be possible to have something that can be taken at much longer intervals?

Pincus: Of course the question of incorporation into food has been brought up before. At the meeting of the International Planned Parenthood Federation in Delhi in 1959, Dr. Bhaba of the Indian Atomic Energy Commission said that economic progress required a 30 per cent reduction of the fertility of the Indian people, and he asked if one might put something in the food which would reduce fertility. Dr. Parkes and Dr. Noble said they knew something that might work (although this was still experimental), but because of the normal variation of individual response to any drug, it might result in some people being sterilized who did not want to be, with perhaps no effect on others who wanted to be sterilized. Therefore voluntary control appears to be the only possibility, even in countries where there is good motivation. Of course in a totalitarian régime one might take a different view, but like Professor Klein I am anti-totalitarian.

The question of "simpler use" comes up every time we discuss this problem. In this connexion, I might mention one experimental study that was carried out in the United States on a substance which, theoretically, would be active at about mid-cycle; it would destroy the fertilized egg. This was offered to a

group of women who were informed that this substance might or might not work; they were instructed to take it from the 10th through the 18th day of the menstrual cycle and they failed miserably—frankly, they couldn't count to 10! Then the man who was conducting the experiment suggested that they take the pill from the 5th to the 25th day—this is a regimen which has been used successfully for anti-ovulatory compounds in Puerto Rico and other places—and this worked somewhat better in terms of taking the pill regularly. (Unfortunately this substance didn't have the effect in the human that it had in animals.) We have found that the only variable to which faithfulness in pill-taking seems to be related is sophistication: the more sophisticated the woman, the poorer she is at using the pill; the more illiterate, the more poverty-stricken the woman is, the more faithful she is. Dr. Eleanor Mears has reported very similar results here in England: people who, using every other contraceptive method have been miserable failures from her point of view, find the pill method easy because they take a pill a day.

Hoagland: In a talk on the contraceptive pill that I gave to physicians in Cairo I pointed out that the new Aswan High Dam would increase the arable land by perhaps 30 per cent, but by the time it was finished, seven or eight years hence, the population of Egypt would have increased 30 per cent, so that the population increase would negate much of the advantage of the dam from the point of view of increase in arable land. Recently President Nasser has come out strongly for birth control measures and family planning clinics throughout Egypt, so that the pendulum has swung in favour of control.

Pirie: I should like to comment on Norman Wright's idea about putting contraceptive substances into salt. If you consider the amount of opposition in Britain to putting fluoride in the water, I feel that the acceptability of such a scheme in a non-totalitarian country is likely to be negligible. Furthermore, one has to consider the variation in consumption. The Swiss, as you probably know, were interested in putting fluoride in

salt, but found that the unevenness of consumption of salt ruled that out completely.

Wright: My suggestion was something like a condiment which individuals could take at will, which would not normally be universally consumed: not, for example, putting it into cereal products, which would be consumed by a whole population.

Parkes: Surely that could be done with existing compounds; you could presumably put norethynodrel into salt as well as into a pill. The whole point of putting things in the food is to reduce the whole population to a lower level of fertility. But on the occasion Dr. Pincus referred to in 1959, in India, it was stated that although that might be the only effective way, it would be entirely unacceptable, however much the country might be in demographic difficulties.

Hoagland: A group of Japanese scientists has demonstrated (and this has been confirmed by an American group) that hot baths (45°C) of 15 minutes' duration, taken three days running, will reduce a man's sperm count very substantially below the number likely to be effective in fertilization; and if this were repeated every 2 weeks a fair degree of sterility could be attained. I would like to know if this is correct and if the application of this would be practicable. I had a debate with some Roman Catholic friends recently and asked whether taking hot baths would be regarded as contrary to natural law. The answer was that it would be, if taken for the purpose of contraception, but if you just took hot baths to be clean that was another matter. I also asked, supposing it were possible to regulate the rhythm method by chemical means so that it was reliable and that ovulation would occur precisely within a period of, let us say, 36 hours, would this artificial control be acceptable, or would this be contrary to "natural law"? It was said this would probably be acceptable. Would you comment on the practicality of regulation of the rhythm by steroidal substances as well as the practicality of the hot baths, Dr. Pincus?

Pincus: The effect of heat in reducing the production of

spermatozoa has been known for many years, but the application of this principle to men and its fairly intensive study originates with the Japanese group that you mentioned. There is no question about the fact that you can reduce the number of spermatozoa markedly in this way. But the really important problem remains unsolved: what is the minimum number of spermatozoa necessary for fertility? As I mentioned, there are steroids which will reduce the sperm count markedly; in fact norethynodrel is one of them. In Puerto Rico we had some volunteers who agreed to take a substance, closely related to the ones I mentioned in my paper, which was mildly androgenic (that is to say, slightly masculinizing rather than feminizing). The sperm count could be reduced to zero with this, but in order to make sure there was no reduction in potency in these men, we gave a dose which reduced the sperm count to just a few million—anywhere from half a million up to perhaps 5 million. And there was evidence that men with even the lowest count could still have offspring. In Puerto Rico this led to some small scandal, because one of the men claimed it was not he but some other man responsible for the pregnancy that occurred, and we dropped the study. Perhaps hot baths would be more acceptable to husbands—I don't know.

Parkes: The difficulty about hot baths is that the raised temperature blocks spermatogenesis, but there will still be a reserve of functional sperm and until these have been got rid of fertility will persist. The integration of a cycle of hot baths and exhaustion of the epididymal sperm would be quite complicated.

Pirie: The hot baths story is a bit older than you think. I have read, I think in Westermark's *History of Human Marriage*[1], that they were used with contraceptive intent in Roman times.

Rather than damaging the testis by heat or other means so that it produces no sperm, I would think that vasectomy would be a simpler and more direct method. The objection to it has been that it is irreversible, resulting in permanent sterilization, but might it not be possible to reverse it if it is done with a more modern technique?

Pincus: Vasectomy has been reversed experimentally by my colleagues, Dr. John Rock and Dr. Celso Garcia. In animals it is easy, if you do the operation properly. In man they have found that it is possible sometimes to undertake repair, but if there is much inflammation at the site of the original operation so much of the tubular apparatus will be destroyed that, at least by their method, it is impossible to restore it. On the other hand, if there is an absolute minimum of inflammation and essentially just the closure of an aperture, its reopening by a very simple means is not difficult. This is a technical surgical matter which in the future I am sure will be solved.

Hoagland: Dr. Rock and Dr. Garcia report 40 per cent now reversible.

Lederberg: We should think also of the possibility of mutations being produced either by the effect of hot baths on spermatogonia or by the cold storage of sperm for artificial insemination. Suppose we set as a "standard of evil" ten times the most pessimistic estimates of the mutagenic effects of fallout; we cannot exclude the possibility that hot baths or cold storage of sperm might have an equally deleterious effect, or even a beneficial one, and it would be a long time before we could collect enough data to be reassuring on that score.

Hoagland: What is the status of "rhythm regulation" at present?

Pincus: I don't know of any studies which do any more than we have done, namely to get a succession of normal menstrual cycles but—unfortunately, from the point of view of the rhythm method—complicated by lack of ovulation. However, there are some new steroids which appear not to inhibit ovulation very markedly and which do regulate menstrual cyclicity. So far no accurate studies have been made on these compounds, but they may turn out to provide the answer.

Szent-Györgyi: I should like to mention an accidental observation we have made recently. We were interested in whether the thymus gland has a hormonal function. The thymus gland is most strongly developed in young animals and

in children and disappears when they become adult. Children are not fertile, and we wondered whether the thymus gland has a hand in this. From the thymus glands of calves we were able to isolate, partially, a substance which increases growth in young animals and also sterilizes animals, both males and females equally. We then found that the growth-promoting substance and the sterilizing factor are different; we have been able to separate them chemically. If the "sterilizing factor" is administered to an adult mouse it has no after-effect. If it is given to very young mice, then it makes the animals sterile for life; the sexual organs do not develop. Unfortunately we have not yet been able to produce the substance in crystals or in great quantity, but I hope that very soon we will be able to do so. All that I can say about it now is that it is not a steroid, since it contains nitrogen. I would like to collaborate with Dr. Pincus in studying this compound further.

Pincus: I read a preliminary account of this finding with great interest. Have you any idea on which phase of reproduction this factor is active?

Szent-Györgyi: We have no idea yet. We only know that if we give this substance to either the male or the female two days before copulation, then no progeny will be produced.

Wolstenholme: It has been suggested that anti-ovulation drugs, by allowing follicles to remain unruptured in the ovary, would prolong the period of life during which women could ovulate and therefore presumably become pregnant. Assuming that there were no unpleasant side-effects still to come and that these drugs were taken almost continuously by women except when they wished to be pregnant, there might be a chance that women of 60 and 70 would have no menopausal symptoms and might be "marriageable" up to a much later period. Is there any validity in this argument?

Pincus: The initial crop of eggs with which each female is supplied declines regularly with advancing age and so far all experimental studies which have attempted to alter the rate of disappearance of the oöcytes (which are the young eggs, so to speak)—except by using X-rays—have failed.

Parkes: That is perfectly true. Ovulation is a minor source of loss of eggs. In most experimental animals if an ovary never ovulated it would alter very little the time of exhaustion of the oöcyte population, and persistence of functional oöcytes would not, I think, postpone the time when the pituitary stopped functioning.

Hoagland: Some women who have been taking the contraceptive pill Enovid have gone through the menopause at the normal time, haven't they?

Pincus: The number is still very limited, but there is no question that several of them gave indications of entering the menopause. On the other hand there are some who continue to be cyclical a little longer than we expected them to. So we cannot make a definite statement.

Koprowski: On the basis of figures of the incidence of malignancies in women taking Enovid and those acting as controls, would you advise women in a country consisting of, let us say, 100 million people to take *en masse* either Enovid or any of the other drugs used in this study?

Pincus: No. That is why we are increasing our observations by a large factor. Professor Klein put his finger on what is the key question in this area: the differences between studies on experimental animals and human beings. In experimental animals this problem has been tackled very intensively; large dosages have been given to laboratory animals, including monkeys, over periods of several years, and the incidence of malignancy among these animals is certainly no greater than in untreated animals. However, one can also raise the question of the human being as a cancer-susceptible individual. It is my impression that the genes involved in permitting the development of cancer in the human are on the whole not present in a great majority of people, and I don't think that the compounds we are using would uncover the genes. But this is still a possibility in old age. The figures which we have obtained on malignancy were acquired in routine examinations. They indicate that there is very little chance of an immediate precipitation of malignancy in large amount. I might add that

among some 5,000 women taking this drug we have yet to see a single case of invasive carcinoma of the cervix.

Hoagland: What about cancer of the breast?

Pincus: The women have not been of the susceptible age.

Koprowski: Women who are now taking oral contraceptives on a continuous basis are 20–40 years of age and their susceptibility to gynaecological cancer can be determined in 20–30 years' time. Only then will it be possible to assess fully the safety of oral contraceptives currently employed. If, by a stroke of ill luck, it should turn out that the use of oral contraceptives has an adverse effect on the incidence of malignancy, equally effective substitutes should be developed and be available, since, by then, an abrupt stop in the massive use of contraceptives may have an equally disastrous effect, although of a different type, on the population.

Klein: Do either the progestins or the other compounds cause malformations? Is there an effect either on the immediate pregnancy or on subsequent pregnancies even in laboratory animals? And have you ever seen malformations in the babies of women who have been taking these compounds?

Pincus: All the compounds that I showed you, except those used in the very latest studies on implantation inhibition, have been administered experimentally to animals and their effects on the embryo have been studied. Several of them tend to cause masculinization of the embryo. The particular preparation that we have worked with, Enovid, is probably not a masculinizing substance. In our studies in the Caribbean roughly 300 women have used the material at least up to the time they have decided to have another child and among these children there has not been a single abnormality, particularly in relation to sexual development. However, Dr. Wilkins of Johns Hopkins thinks that the use of one of these compounds, 17–ethinyl–19–nortestosterone (ethisterone), should definitely be avoided early in pregnancy, since he has seen a number of cases of pseudohermaphroditism (slightly virilized girls). Much more work will be done on this in the future but the experimental work with animals so far indicates that the ovulation-

inhibiting dosages are so low compared to the dosages necessary to cause these effects on the embryo that the chances of producing an effect on the embryo are very remote.

So far as other side effects of these compounds are concerned, these drugs act like hormonal steroids and the side effects are those which one would attribute to hormonal steroids; that is, one might expect to get effects on the pituitary which in turn are reflected on ovarian function and even on adrenal function. However, here again the dosages which inhibit ovulation are so low that no very marked effect on the other glands of internal secretion has been observed, at least so far.

Lederberg: Dr. Parkes, you showed a rather startling curve of alteration of sex-ratio in the 1901 series. There was a drop from 100 at birth to about 90 per cent ratio of males at marriageable age. Are there mortality statistics that would corroborate that?

Clark: The South African war was on.

Parkes: The figures I think are all right, but mortality certainly does not account for the whole of it. Emigration was undoubtedly a big factor.

Hoagland: You mentioned that during wartime—and especially during the first world war—the number of males went up relatively and then you mentioned later that younger marriages might be involved here. I am surprised that this would make any difference in the sex-ratio.

Parkes: Younger marriages produce more males relatively, and the age of marriage decreased considerably during both war periods.

Bronowski: Younger marriages and first children both produce more males.

MacKay: If males outnumbered females in the ratio 105:100, this would only mean that in every circle of 41 people, one (on the average) might be partnerless for this particular reason, namely that he was of the "excess" sex. In practice this factor would be embedded in so many others that affect people's chances of marriage, that I wonder if we are not making too much of it. At the individual level it would be hardly detectable.

Parkes: It depends on whether or not an equal number of males and females fail for some reason to get married. But in any case the sex-ratio, as you say, is not very catastrophic at present. It certainly wouldn't set up social pressures of a kind which would change the whole social system and lead to polyandry. But we are not at the end of the tendency for more and more males to survive to marriageable age.

Haldane: What happens if you make allowance for the fact that on the whole husbands are three or four years older than the wives? I think it would even out much of the excess of males. On the one hand there will be more females surviving to a younger age, and secondly, there will be the effect of the expanding population at the present time. Perhaps our habit of marrying a woman slightly younger than ourselves, or a husband slightly older, may be an adaptation to this excess of males, and have the effect of approximately balancing it.

Parkes: The custom of marrying a wife slightly younger is, according to my understanding, of quite ancient origin, and certainly was common during the last century when there was an overall excess of females of marriageable age. Of course, this tendency may now be increased by the present slight excess of males of marriageable age, and, according to the demographers, that is going to become a vicious circle as the excess of males increases.

Trowell: There is a very long history behind this practice of men marrying women younger than themselves. It also occurs in polygamy and most areas of the world were polygamous until a few thousand years ago. In polygamy the excess of married women over married men is only possible if women marry at a younger age. This is still true in Africa.

Coon: Have you considered the racial difference in sex-ratio? Among Berbers it used to be that the children of a man with four wives showed a much higher sex-ratio than those of the man with three wives, and so on down. But south of the Sahara the Africans, who were equally if not more polygynous, had a low sex-ratio. Does that mean that in the future the

excess white males will end up by marrying negresses, because there aren't enough white women?

Parkes: I doubt whether the question of polyandry or polygyny influences the sex-ratio of the offspring in any scientifically detectable way.

Coon: Not even when it involves marrying younger wives?

Parkes: That might be an indirect effect.

Haldane: My colleague S. K. Roy finds among goats a very significant excess of females among single births and males among twin births. This appears to me to be a novel observation, but perhaps Professor Parkes will tell me that it has been known for fifty years.

Parkes: Not by me, sir! The only explanation of this observation that I can think of is that the higher sex-ratio in identical twins might result from a greater probability of splitting in the case of a male blastocyst.

Haldane: There is no significant excess of like-sexed twin pairs suggesting monozygosis.

Parkes: Then that disposes of the only explanation I have to offer.

Lederberg: Dr. Parkes, would you elaborate on the technicalities of the separation of the X and Y spermatozoa by physicochemical means? I know about Gordon's and Schröders' earlier work on separation of male and female sperm by electrophoresis and I wondered whether their claims had been substantiated.

Parkes: I think someone in England has obtained the separation of rabbit sperm into two distinct groups, but without a biological test. In general, efforts to repeat these experiments have not been successful—possibly because electrophoresis is a very complicated procedure, so that it is difficult to reproduce an experiment exactly. However, Lindahl in Sweden, using a different separation method, namely, differential centrifugation, claimed to have produced a fraction of bull sperm which, on insemination, resulted in the birth of eleven consecutive bull calves. That was very promising, but so far as I know, Lindahl has not done any large-scale studies. To my

mind, all these studies should be repeated on a much larger scale.

Bronowski: On a purely theoretical point: Professor Parkes asked in his paper if there is any significance in the fact that the sex-ratio is roughly 1:1. There are two parts to this question. One part, of course, is answered by remarking that if you start with a population with any sex-ratio at all, then because males contribute X and Y chromosomes in equal numbers, you will move to an equalization of the sex-ratio. That is a pure question of mechanics.

Lederberg: This is begging the question. The Mendelian expectation is a sex-ratio of 1:1 at conception. This appears to be very far from true. Instead some selective process causes the sex-ratio to approach 1:1 at maturity. The problem is the physiology in the evolutionary mechanism of this adjustment.

Professor J. F. Crow[2] has pointed out a very simple formulation of the population dynamics of the sex-ratio. If at the reproductive age one sex is less numerous, individuals of that sex will have a greater average number of progeny than individuals of the other sex. Then an individual who produces more offspring of the scarcer sex will transmit the corresponding genes to more grandchildren than the individual who produces the average ratio. Thus the genes controlling sex-ratio will be selected to the point of equality for the sex-ratio at reproductive age.

Bronowski: Secondly, there is a more subtle part to the question, which Professor Parkes was also asking: Is there any advantage conferred on a species with a sex-ratio near to 1?

Parkes: Is there any advantage, that is, when there is such a large difference in reproductive potential between the two sexes?

Bronowski: There is an advantage, if you call it such, an advantage in variability. Mutation doesn't produce variability in itself, it only produces the potential to variability. Now if you have equal mutation rates in males and females, then you take the highest advantage of this, if variability is what you want, by having an equal sex-ratio. (In physics this principle

is called the equipartition of energy.) You can see the logic of this by taking the opposite extreme: if you have equal mutation rates but only one male to the whole population of females, then you are not getting maximum variability from the mutation rate. Presumably what nature is trying to do is to produce high variability.

Parkes: I was hoping that somebody would produce a valid reason for the existence of us males.

Haldane: I should like a formal proof of Dr. Bronowski's theorem. Such theorems sometimes turn out to involve some remarkable assumptions.

MacKay: This notion of efficiency is apt to be troublesome in a biological context unless we ask explicitly, efficient with respect to what? Thus when Professor Parkes commented on the inefficiency of maintaining a million tons of redundant male bio-mass, he presumably meant "efficiency with respect to human meat production". Once made explicit, this thrusts us back to Sir Julian's question—what are humans for?

Bronowski: The definition in my theorem is, efficient with respect to the exploitation of the potential variability which mutation creates.

Pirie: I agree that this excess of men isn't very alarming and variations in the laws of a country could possibly compensate for any chaos that might be introduced. But if it should become alarming we might direct Dr. Pincus back to some of his earlier studies on parthenogenesis (virgin birth) where you get female offspring only. If we could get parthenogenesis going in man we would be able to produce any extra number of women who are required to even out the ratio. Now, having said that flippantly, I am going to ask more seriously, what is the present status of parthenogenesis in mammals?

Pincus: The present status is not very good; it is a very inefficient process by the methods we have used. Dr. Chang in our laboratories has increased the rate of parthenogenesis in treated rabbit ova by a large percentage, but the eggs only develop to a very early stage; the yield of mature animals is negligible.

There is another avenue to sex determination which Professor Parkes might have mentioned, and this is the effect of the steroids on sex determination or on other sex-determining factors. It is well known that if you take frog eggs and immerse them in an oestrogen solution you get 100 per cent females. Recently in our laboratory we have been immersing rabbit eggs in oestrogen solution, and so far we have 90 per cent females.

Medawar: I should like to question Parkes' belief that we are only at the *beginning* of a tendency for the sex-ratio to increase, and that we can look forward to a still greater preponderance of males. I don't think that is true. I think the present tendency for the sex-ratio to increase is due to a number of demographic tendencies which are self-limiting. Parkes mentioned one of them—the tendency towards a younger age at marriage; a second one, which he didn't mention, is probably equally important, namely, the tendency for families to be completed earlier and earlier in married life, and that is also a self-limiting factor; the third tendency is differential mortality itself, which has hitherto favoured females throughout the whole of life, anyhow from birth onward: that is also self-limiting because mortality up to the ages at which most people marry is in fact getting somewhere near as low as it can ever be. So I don't think that we need fear that the sex-ratio is going up to ludicrous proportions over the marrying years.

Brain: Another factor, of course, is homosexuality. We don't know the incidence of it, but apparently it is substantial enough, if there is a differential between the two sexes, to counteract completely the other comparatively small figure.

Comfort: The incidence of male homosexuality might also be influenced of course by the unavailability of females in the future.

Crick: In the light of all that, Professor Parkes, could you estimate, for 10 or 20 years ahead, what the sex-ratio is going to be, making reasonable extrapolations in the way that Medawar has pointed out?

Parkes: So far as infant and postnatal mortality is concerned, as Medawar said, we may be getting near the limits of decrease,

but there is still the very large prenatal mortality to consider. And if one accepts that it falls differentially on males, then its decrease will further increase the number of males at birth.

Medawar: It depends what causes those deaths of males before birth, doesn't it? If they are genetic deaths, due to chromosome aberrations of some kind, it is probable that they won't be within reach of medical treatment.

Parkes: I agree. But in this very large prenatal mortality—and I am thinking right back now to the time of implantation, not merely to the time when overt abortions occur—what is the evidence that genetic non-viability is a big factor?

Medawar: I am not saying there is evidence in favour of this idea; only that we have no evidence against it.

Lederberg: I predict that in 10 or 20 years we will have found a simple chemical method for biasing the sex-ratio. But what would happen then? Suppose the sex-ratio were under voluntary control, and suppose there were a small excess of males, would we have to anticipate a sudden increase in the sex-ratio even over that? Would there be a "business cycle" with a substantial degree of inertia and overshoot from generation to generation? These are important questions.

Parkes: With the present social set-up, and I keep on emphasizing that qualification, I think the result of voluntary choice, with a certain amount of overshoot and so forth, would be a sex-ratio much the same as we have now.

Lederberg: What is the evidence for this? Do we have any data on people's attitudes or choices in any range of our society which would enable us to write the econometric model of the future development of such choices? This is the urgent business of this kind of symposium.

Crick: Surely it would be quite easy to obtain; you have only to ask different classes of people, who have had different numbers of children, what sex they would like their next child to have if they had a choice.

Lederberg: You must do that, but you must also find out how they behave as well as what they say they want. And you must anticipate what this behaviour will be as a function of the

actual sex-ratio and its age distribution. To revert to Professor Crow's argument, if there is a *hereditary* disposition for choice of one sex, the ratio will even out through natural selection of the counterbalancing genes (or traditions).

Clark: There is some statistical evidence about this. I am speaking as rather an abnormal case, as a father of eight sons followed by one daughter. The mathematical probability of that can be worked out. Gini in Italy counted the number of such families and also of the converse—eight daughters followed by one son—and found that the latter were far more frequent; so that in Italy there is preference for sons. Parkes raised the point about young mothers having more sons. The crude statistics indicate, as Bronowski mentioned, that first births also show a higher male proportion. Is that fully explicable by the age of the mother, or does sequence of birth make some difference?

Parkes: There is a correlation of course, but just how great I cannot say.

Medawar: There is another variable, namely, the age of the father, because the children of younger mothers tend also to be the children of younger fathers. I believe that the age of the mother as such, and the parity of the mother as such, are not important variables, but that the age of the father is.

Bronowski: I can add a footnote to what Colin Clark has just been saying about the statistics. There is some statistical evidence to answer Crick's question, but it is indirect. If you take the distribution of male and female children in large families, then you find that, in families of 3 or 4 or 5 children, the distribution is random; runs of all boys or all girls occur only as often as they would if we were tossing heads and tails. But when you get to families of 6 or 7 or 8 children and upwards, then there are too many runs of all boys or all girls. This is a clear indication that parents with one-sex families go on having children because they want to have a child of the opposite sex—either sex. I have had four daughters and no son, and I assure Lederberg that if I knew of a chemical which would ensure that I should not have another daughter I would use it!

MacKay: Any attempt to predict public preferences in these matters will have to reckon with the effect which publication of the prediction, or action based on it, can have on its validity.

Crick: I doubt if the publication would have as much influence as that due to the actual changing sex-ratio of the population, though I wouldn't like to say whether it would be a stabilizing influence or not. Moreover, surely this is partly a cultural phenomenon. There are countries in the world where at the moment sons are very desirable and daughters are not valued so highly.

Brain: The one thing we seem to agree about is that we males are highly selected survivors.

Growth and Development of Social Groups

CARLETON S. COON

The term "social group" is a broad one and has many definitions. For this reason, and because there is no accepted method of measuring social phenomena, the so-called exact scientists tend to look down their noses at sociologists and social anthropologists. But the existing confusion and vagueness need not be perpetuated. Some solid scientific work has been done in the field of human relations, only it is not at present fashionable.

As long ago as 1909 Van Gennep published his little-noted work on the Rites of Passage[1], rituals which automatically take place in any society to allay the disturbances to all persons concerned when one individual goes through a critical change in his or her position in the social group, from birth through puberty to marriage, and eventually to illness and death. The "persons concerned" include not only the individual undergoing the change but also those who interact with him the most frequently, including his immediate family.

In 1922 Radcliffe Brown published[2] his explanation of the various rituals which the Andaman Islanders used to perform both in the individual life cycle and in the changes of seasons, and he was particularly concerned with the way in which certain substances were selected as symbols of each kind of disturbance. For example, hibiscus leaves, which were used in the context of situations associated with a number of disturbances were automatically selected for ritual use.

During the 1920s and 1930s Malinowski[3] studied the ways in which the equilibrium of social groups in the Trobriand Islands was maintained, and in 1942 Eliot Chapple and I discussed the whole subject of social equilibrium in a textbook which

attracted little attention and which we are rewriting[4]. In it we added the concept of Rites of Intensification, in which whole groups of people conduct rituals together to allay disturbances due to external forces, such as war, weather, and seasonal change.

As early as 1935 George Zipf demonstrated[5] that the length of words in a language are, other things being equal, a function of their frequency of use, and in 1948 I showed, in a study of the Albanian Ghegs, that the ideal choice of a marital partner is the one that will cause the least possible disturbance to all persons concerned, including of course the kinfolk of the bride and groom, and not just the marital partners, who have little to say about it.

These illustrations have shown that the equilibrium of a social group seems to follow the law of least effort, in a mathematically simple manner, apparently more nearly comparable to the ways in which equilibria are maintained in physics than in biology. Our societies seem to be simpler than we are.

Before trying to define the term "social group", we first need to consider the definition of one of its components, the *institution*, a word of many meanings used here in the sociological sense. To quote from my own *Reader in General Anthropology*[6]: "in its simplest form an institution is a group of people who meet together in isolation often enough, regularly enough, and long enough each time, to do something together intensely enough and emotionally enough so that as a separate entity the group builds up its own set of rules, its own equilibrium, and its own structure."

In every society each individual belongs to more than one institution because a biological family is an institution and every viable social group includes more than one simple family. A social group is, therefore, a collection of human beings who habitually interact with each other more than they do with outsiders, and form, in a sense, a population.

The most primitive peoples alive, who hunt and collect their food, live in breeding units of about three or four hundred individuals, and these units are also biological populations. At

the same time they are nations. People who live by food production and industry are members of nations which, as a rule, contain more than one breeding population, and the maintenance of equilibrium is to that extent a more complicated business.

HUMAN EVOLUTION, PRE-SAPIENS BEHAVIOUR, AND THE DIFFERENTIATION OF INSTITUTIONS

During the vast expanse of the Pleistocene, in which man evolved, breeding populations and nations were small. Only during the past eight or nine millenia can any have grown much larger. It may therefore be that *Homo sapiens* is primarily adapted to living in small, simply organized, face-to-face groups, and this is perhaps true of the vast majority of mankind today. In much of Europe, the Middle East, China, and India, villagers still have the same kind of relationships that they have had since the beginning of the Neolithic, and even in cities everywhere, the ordinary people live in small, more or less well defined neighbourhoods. In every society, however, there have been exceptional individuals capable of interaction on a large scale. They have been the leaders in many kinds of activities, the creators and maintainers of large and complex institutions.

To arrive at this condition *Homo sapiens* had to evolve out of his parent species, *Homo erectus*, and this process was probably primarily concerned with human relations, because no sharp break can be seen between the two species in technology, as seen dimly through the evidence of stone implement types, kinds of animals eaten, and ways of breaking animal bones. Even fire was used by *Homo erectus*, at least in China. The rise of *Homo sapiens* is indicated almost entirely by changes in the size and apparent structure of the brain and probably of the pituitary. There is some evidence that *Homo sapiens* matures later in the human life cycle than his ancestor, and lives longer.

It would be unwarranted to dwell at length on the social behaviour of *Homo erectus*, who has left the earth forever, except to remind you of a few firm points. He hunted, and hunting requires group activity. He fought his fellows, as evidenced by

the virtual universality of severe head wounds in *Homo erectus* skulls, including those of both sexes.

By analogy with the behaviour of other primates and indeed of many animal species, and through the recent work done on instinctive behaviour in other animals and man[7], we now know that human beings really are born with built-in drives, although some are unco-ordinated. For example, like us, chimpanzees have to be taught how to copulate.

As human beings became increasingly competent in technology, so that everyone did not need to seek food from dawn to dusk, a division of labour arose between persons of different ages and both sexes and eventually between grown men specialized in different skills. Out of these specializations grew institutions beyond the scope of the family. The chief and his followers became a political institution, the knapper of fine flints and his clients an economic institution, and so on.

But the number of kinds of institutions is limited, because those that arose in this fashion seem to have followed the lines of instinctive motivations. The family is based primarily on sex and care of the young; the economic institution on hunger, thirst, and the need for shelter; the political institution on the demarcation and defence of territories; the religious institution on curiosity, fear and deprivation of interaction; and voluntary associations on the so-called peck order. Each kind of institution has its characteristic patterns of interaction both between its members and with outsiders.

ENERGY CONSUMPTION AND INSTITUTIONAL COMPLEXITY

The complexity of institutions in a society is a function, other things being equal, of man's conversion of energy into social structure. He has done this through the progressive use of energy, in technological procedures[8]. The sequence starts with the use of fire and culminates with that of atomic energy, and will lead to the use of other kinds of energy known only to God and the physicists. Technology in the sense used here is not limited to economic institutions but permeates all others. Families use dishwashers, presidents fly in private airplanes,

and muezzins call the faithful to prayer through loud-speakers.

The principal technical vehicle through which institutions are able to grow to immense populations is that of communication. From smoke signals and message sticks to post-horse couriers, to trains and telegraph clickers and television sets, is a familiar progression. In times of crisis monarchs, presidents, and prime ministers are seen and heard by entire nations, just as the members of a Neolithic village used to see and hear their chief.

During the course of history the numbers of institutions have increased more rapidly than the numbers of people concerned because each person comes to participate in an increasing number of institutions. On the other hand there is also an opposite tendency for the number of nations to decrease just as the number of separate languages decreases. But this second change does not work as a simple progression. Empires break up under the impact of new media of communication and dozens of small states temporarily arise. Nationalism is apparently a necessary prelude to internationalism, or decay, or whatever is in store for the new nations which now outnumber the old in the United Nations.

A further stage is seen in the efforts of the old European nations to unite, and to create a powerful third force between the American and Russian colossi, which grew up essentially through the occupation of previously nearly empty spaces.

CONTROL OF SOCIAL EQUILIBRIUM

Whole societies, whatever their sizes and degrees of complexity, need controls to ensure the maintenance of equilibrium, and control comes in several forms. One is ritual, the repeated use of symbols and symbolic procedures in any type of activity. Without ritual there would be little discipline in an army, and the public appearances of heads of state are usually shrouded in ritual. Ritual also creeps into industry, as when a retiring employee is given a gold watch in the presence of his fellows, and ritual is of course the chief business of the religious institution.

Warfare between neighbouring groups of people is another well known means of preserving equilibrium at home, and this is particularly true in regions where there is an imbalance between women's work—gardening—and men's work—hunting, in the absence of domestic animals. Such warfare was a seasonal practice among many tribes of American Indians.

All peoples also play games, which serve as a substitute for warfare in providing an ordered pattern of interaction, usually accompanied by ritual. The original Olympic games made it possible for the independent Greek city-states to coexist peacefully, at least during the times when the games were held. The current space race, in which semi-divine astronauts whirl around our planet, may be viewed as a very expensive kind of game which takes some Russian and American minds off greater problems, while leaving spaceless nations uneasy.

Law, of course, is the prime arbiter of the internal stability of states and nations. The law states explicitly which actions may or may not be done, and the actions that are forbidden are precisely those that upset the smooth patterns of human relations within a society. Among very primitive peoples there is no code of law, only a general agreement about what has disturbed the group in the past, and what to do about it. Laws vary as cultures vary and laws change, if tardily, as cultures change.

An equally fundamental means of maintaining orderly relationships within societies is education. In simple, illiterate societies there is usually a large enough group of boys or of girls to form an age grade, which in itself is a kind of institution. The classmates play together, learn from their elders by imitation, and go through puberty ceremonies together. In these ceremonies the basic rules of behaviour toward persons of different ages and the other sex are imprinted, often by shock treatment including fasting, vigils, and sensory deprivation. We are only beginning to understand the effectiveness of these didactic techniques.

As societies grow in size and complexity so do the educational institutions. Formal schools for an élite arose with cities, and

the idea of mass education in large communities has appeared late.

In the most successful civilizations of the past it was enough to train from infancy an élite whose members could assume leadership as needed, and this system permitted much individual cultural variation in the provinces and among conquered peoples, each of which was allowed to keep its own identity and morale. Trying to educate everyone with identical curricula cannot produce a homogenized mass of tranquillized subjects nor can it maintain the quality of a nation. For every hidden genius that it extracts from an under-privileged background it fosters a dozen rebels. And scientists who know nothing but science can imperil the safety of the world.

EVOLUTION AND DIFFUSION IN THE GROWTH OF SOCIETIES

In various parts of the earth unique civilizations have grown up more or less independently from simple beginnings. Middle Eastern civilization, Mediterranean civilization, and Western European civilization represent three stages, moving westward into newer grounds, of our own tradition. Chinese civilization is another, with branches in Japan and elsewhere, and in America the conquistadores found autochthonous civilizations in Mexico, Guatemala, and the Andean countries, both in the highlands and on the coast.

No civilization grows up in absolute isolation. There are always peripheral contacts which diffuse one technique, ritual, or other trait from one centre to another. Such autochthonous civilizations grow up in a state of balance. Their institutional growth mirrors their technological advances in a steady fashion. Old traditions cling on and old practices gradually assume new rôles. These are, in short, nuclear cultures.

At the same time, in equally or more isolated parts of the earth, other nuclear cultures grow and evolve in a harmonious fashion but at a much slower rate. These are the primitive cultures of stone age man preserved by the miracle of geography into modern times.

In between these two polar types of culture, clinal societies

are found. In Africa, for example, many tribes went directly from the Neolithic to the Iron Age without the intervening use of bronze, and straight from simple hunting and gathering to herding cattle. In India primitive monkey hunters and root diggers hid in the forests for millenia while a parade of successive civilizations passed by on the plains below. In Africa the iron-working Bantu, having obtained new sources of food, exploded eastward and southward, from their West African home, by-passing the Pygmies, while in India some of the simple hunters and grubbers came down from their leafy retreats to become specialists in humble occupations, and also outcastes.

In the well-known history of the Germanic invasions and the terminal history of the Roman Empire a similar upset took place, for a number of reasons, one of which was the export of technical skills from Rome to the colonies, which came to need contact with the capital less and less. When the political institution weakened, the church took over and a degree of equilibrium was restored in a new way. It took several centuries for western society to get back into the semblance of a well-balanced web of institutions.

THE RELATIVE FLEXIBILITY OF SOCIAL SYSTEMS

Old-established systems which have had the advantages of a steady, balanced growth tend to be resilient and flexible. They absorb and recover from blows. The state does not usually dominate the church, nor is everyone madly passionate about games or war. A multitude of optional occupations and of voluntary associations gives room for the varied outlets of different kinds of personalities, and a class system, overt or covert, permits the growth of a sometimes inconspicuous élite.

What preserves the serenity of such civilizations is a harmony between the duration of the individual life cycle and the rate of cultural changes. The culture must change or it will rot. On the other hand, as people grow older they may wistfully note that things are not as they were before, but in a well-modulated society the rate of change is not swift enough to cause more than a little sadness associated with diminishing energy and

hardening arteries. The things that we learn first imprint themselves the most firmly and have the most to do with our emotional life. These are family, territory, and status. They cannot be easily unlearned, and as the roots of cultural change lie in technology, these other things lag behind and move more slowly, accommodating their pace to that of the life of the individual.

The rate of change in any social system can be accelerated by two means, or by a combination of both. One is the diffusion of new techniques from one cultural centre to other peoples, and the second is the over-rapid growth of technology towards the climax of a cumulative cycle, such as we live in today. The first is a commonplace of history, the second unique in our own age.

When a peripheral culture area is swamped by the introduction of new techniques, a number of things can happen. A very primitive food-gathering people may be driven into barren wastes, if any are available, as in the case of the surviving South African Bushmen. If there is no escape they succumb to a combination of diseases from which they have no immunity and a neuroendocrinological dysfunction, like that found in animals subjected to crowding. Crowding affects reproduction rates as well as the will to live in a new, incomprehensible, whirling social order, in which old values are discarded and the wisdom of the ancients turned into prattle. To these disorders may be added nutritional shock by the replacement of habitual wild foods by flour, sugar, tea, tobacco, and alcohol. For people subjected to such invasions of privacy and indignities by modern, civilized intruders, there is little hope of genetic survival except by peripheral absorption into the lower fringes of the invading population.

Peoples with a less vulnerable food supply, such as fish and garden products, who see vast shiploads of new kinds of food and of machinery landed ashore for the use of invaders, may pass into the dream world of a cargo cult in which their leaders tell them to destroy all their own cultural paraphernalia while awaiting the arrival of imaginary shiploads of foods and goods.

These cargo cults, a special problem for administrators in New Guinea, have had their parallels in the rise of new religions, based on revelations, in more advanced cultures during times of stress, in the rise of Christianity and, even more clearly, in that of Islam.

Another type of disturbance affects the vast populations of the so-called "developed" nations. Among them technological change has moved through time at a measurable and predictable rate of acceleration until now it marches too fast for the toleration of the average individual human being in his lifetime. The consequent changes in institutional structure are too vast for many people to bear.

Russia is a particularly vulnerable nation from the standpoint of brittleness, for several reasons. The Russian empire includes large populations of Muslims and Buddhists as well as of Christians, which makes religion a divisive force. Therefore religion had to be downgraded if not abolished. In order to compete with America and Western Europe in agriculture and industry the rate of technological change had to be speeded to a maximum. To keep people quiet while going through such changes, communication had to be strictly controlled, particularly international communication. To these ends the political institution had to be hypertrophied at the expense of all others, and the cushioning qualities of the other institutions have been correspondingly reduced or lost.

But even in the most flexible of highly developed civilizations and governments, there is no time for natural selection to screen out those who can or cannot tolerate the disturbances attendant on technological acceleration alone, and the current population increase adds more to the spectre of chaos. In other words, disequilibrium is spreading from the peripheries of the world, where we carried it, to the centres of world civilization, in which we live.

SOCIAL EVOLUTION AND ENVIRONMENT

According to the calculations of physicists and generals dealing in the problems of atomic warfare, energy is becoming

as nearly infinite as it need be to cancel out life, time is shrinking to a few ticks of the clock, and space is growing as inconsequential as the surface area of a postage stamp. Yet as long as the major part of the face of the earth remains intact, variations in environment will still be with us. Arctic wastes and parching deserts will still be marginal areas to a certain degree. The requirements of keeping warm or cool and the difficulties of finding food have kept some of the world's cleverest people, the Eskimo and Lapps, on a very simple institutional level, and it is not easy to imagine any technological changes that will make the icecaps and deserts of the world anything more than expensively maintained colonies of captive workers as in Greenland, Antarctica, and the Arabian oilfields today. The best lands of the world will continue to be centres of social complexity in the foreseeable future, if we think in terms of people rather than of machinery.

RACE AND SOCIAL EVOLUTION

I have left to the end the most troublesome—and least rationally handled—aspect of the total problem of social evolution, that of race. Yet it is a real problem and must be faced if we are to do anything but chat about the future of man. Since the time of our first knowledge of *Homo erectus* our genus has been divided into geographical races adapted in varying fashions and degrees to heat, cold, altitude, and disease. These adaptations remain[9]. How long will the Communist Chinese be able to survive and reproduce their kind in the thin air of Tibet? Will the genetic superiority of native West Africans over White men, which has kept the latter out for centuries, be lost when all the malaria-carrying mosquitoes have been stamped out with millions of tons of DDT? If the races of man stay where they are best adapted, it creates much less trouble than when they move into each other's territories.

And, more importantly, are all peoples equally suited, in a neuroendocrinological sense, to live under the regimentation which is bound to come in a vastly overcrowded world? These are questions that I cannot answer, and the very mention of

them is considered indecent in my country. Do the minds of all races work in the same fashion, do not their emotions differ with differences in their hormonal peculiarities, and is it not possible that cultures vary to a certain extent in terms of these variations? These questions require research, and the results may mar the vision of a single world culture. People are genetically and culturally different, and short of a global police state run by persons yet to be determined, entrusted with the power to perform chromosomal surgery and interspecific transplants, they will remain different for a long time to come. If the world is to become united, the union must be a loose confederation of very different units, or it will not long endure.

Man's Relationship to His Environment

ARTUR GLIKSON

I AM going to use the term "human environment" to describe the space which surrounds human movement, work, habitation, rest and interaction—towns and villages, settlement influence areas, the rural and the accessible virgin landscape. This environment is generally defined as a set of biological and physical facts in space, as modified by man.

Nothing would distinguish the principles of man's relationship to environment from those of other species, were it not for the fact of his own evolution. Man, a powerful agent of change in space, himself undergoes change in time. This fact transforms his rôle in any natural community into a dynamic, unstable and often contradictory relationship unique among species: dynamic in space—the give-and-take relationship with the earth and its life—and dynamic in time—the recurrent change, destruction and renewal of such give-and-take relationships in reference to new situations. All established settlement regions show evidence of the continuous imposition of new environmental patterns on top of the old—of a temporal dimension in settlement structure.

INTERACTION OF HUMAN AND ENVIRONMENTAL EVOLUTION

The elucidation of human evolution would provide a key to understanding the changing shape of human environment. But human evolution itself cannot be understood without reference to the interaction of man and environment. A distinction is generally made between the cultural and biological aspects of human evolution. Whereas biological changes are hereditary, cultural acquisitions, such as knowledge, ideas, tools

and the environmental heritage can be misunderstood, forgotten or rejected by new generations. Though the two processes make up the changing human constitution, we can discern in man no direct connexion between biological and cultural evolution. However, through man's environmental relationship, an indirect connexion between them is established: first, through the impact of cultural evolution on the biology of man's environment, effecting both qualitative changes in and distribution of plants, animals, water, air, soil, micro-climate, materials, etc.; next, through the decisive influence of these changes in their turn on the total psychophysical position and function of man in life.

By observing and interpreting the evolution of man's relationship to environment, we gain important clues to the profound significance of cultural evolution for the human constitution. In environmental change, cultural facts are converted into biotic realities, while biological conditions mould human culture in their turn; human and environmental evolution become interacting processes of change, constituting a whole life-system. To comprehend the system, we must study alternately its human and environmental components, consider both biological and cultural aspects of evolution, and note their interconnexions whenever they appear.

ENVIRONMENTAL EVOLUTION AND ENVIRONMENTAL CHANGE

When observing the human environment, we are always confronted with its dual determination. It is conditioned by human life, and it conditions man's functions and development. But the evolution of the human environment appears as a sequence of stations, on each of which a high degree of integration of community and environment is realized and maintained over long stretches of time. Communities may come close to identifying themselves with their environment. In various ancient farming societies, such as the South-American Ayllu and the widespread Asian Savah, community and environment were named by the same term. Such knowledge can help us to understand past environmental orders; it can also give us

confidence in future when such an harmonious man-environment relationship might be re-established.

When we wish to effect change in the man-environment relationship, the realization of its mutuality is a necessary starting point. But the truth that man and environment determine and are determined by each other is not sufficient to provide guidance for man's modifying actions. On the contrary, this knowledge is liable to hide the fact that the incentive to change results from the experience of an incompatibility between the environmental situation and the human situation.

Environmental change is motivated either by the existence of free human energy, not needed for the maintenance of existing communities, or by a disturbance in biological or physical equilibrium. A surplus or a deficiency of population or resources, migrations or wars, may initiate a process of environmental change. Such conditions urge communities to "reflect" themselves in new ways upon the surrounding biota and landscape, to introduce different types of land use and to reorganize their cultural habitat. But, in the course of this activity, they encounter reciprocal environmental influences which modify their goals and way of life.

Environmental disequilibrium stimulates thought and action. Yet no definite programme of action can result from the mere awareness of estrangement from environment. The disturbed relation, therefore, urges man to search for guidance on a different level. So long as such guidance is not found, men have no choice but to justify or permit arbitrarily any environmental effort or neglect as a "natural" or a "human" process.

Guidance for environmental modification and cultivation ensuring a balance was gained in the past by instincts, or by myths, or religions which established doctrines about man's situation and responsibilities in the universe. Our understanding of past environmental relationships remains incomplete, if we disregard such spiritual bases. In our time we must seek for such guidance, first of all in what Aldo Leopold called "a land ethic . . . reflecting the existence of an ecological conscience" and evolved as "an intellectual as well as emotional

process"; this ethic, combined with a social conscience, would derive from a sympathetic attitude to life and culture in its various manifestations, leading man to realize his obligation towards the biological context as well as to humanity. Secondly, environmental modification must be guided by an environmental art—an architecture—which not only integrates experience, knowledge and ethics in creative design and development, but which in the very act of integration and design becomes exploration of environmental realities and values. In thus adopting the function of responsible agents of natural and environmental evolution we may hope at times, to fulfil our humanity.

VARIETIES OF THE MAN-ENVIRONMENT RELATIONSHIP

Under more or less permanent climatic and geological conditions, and barring unusual biological events, there exists only one ecological climax development in a landscape which is devoid of human influence. But in the history of the humanized landscape, there are many "climax" developments because of the changes in the ecological rôle fulfilled by man. To the extent that a species is characterized by occupying a particular position and fulfilling a specific function in an ecological community, man, by virtue of his cultural differences and their development in time, represents (as it were) a multitude of different species. In respect to the environment man is not a consistent biological unit preserving its identity, but an organism in the process of change. We must therefore consider a wide range of environment contexts. In the following pages I shall give examples of such contexts, as related to human mobility, sedentariness and urbanity. In these brief descriptions, a community's characteristic manner of using land, space and time is shown to emerge from or to result in a pattern of human rest and movement in the landscape. This pattern modifies nature, forms the humanized environment, and implies the creation of specific values in the man-environment relationship.

Mobility

The hunters' and collectors' society must be a starting point for any study of the development of the man-environment relationship. Human communities, like other animals, keep moving from camp to camp to replenish supplies of food and water. In their natural ecological state, most regions can sustain human life for only part of the year. Man's main energy "investment" consists, as a result, of his own movement from one favourable ecological context to another—and as these optima change with the seasons, it can be said that man maintains his existence by a wise use of time rather than of land. In this context the landscape is formed by ecological systems in which man is no more than a temporary partner. To leave the land alone and to follow the sun is the rationale of man's mobility. Its scale is almost unlimited by natural regions, bringing man into close contact with a wide range of conditions and situations. Inter-tribal contact is casual, and the general population density is estimated to be in some regions as low as 0·2 persons per square kilometre. Space is experienced essentially as exterior, a seasonally changing unbounded condition. Just as the flow of biotic energy moves continuously with the seasons through the ecological "chains" of the landscape, human mobility likewise has no proper centre, though certain locations may be seasonally revisited. The apparent exception to this order of mobility—early riparian settlement—proves the rule, for here we find an exceptional dynamic environmental condition: the regular movement of a whole eco-system, the river, combined with a favourable climate enabling man to stay in one place, while enjoying (as a beachcomber) an ever-replenished supply of food, materials and water (Fig. 1).

Sedentariness

Sedentariness is perhaps the most astonishing biotechnical "invention" and the most successful revolution ever carried through in man's relation to his environment. The conditions for sedentariness are the acquisition of biological knowledge and

Schematic presentation of relationships of communities and environment under conditions of mobility, sedentariness and urbanity.

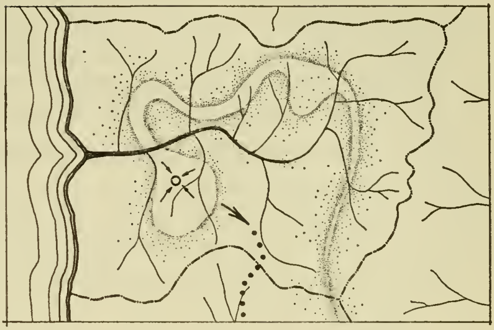


Fig. 1. Mobility. The landscape of a watershed basin as modified by land- and time-use of prehistoric hunters' or food collectors' societies moving from camp to camp: integration in a given web of life.

Fig. 2. Sedentariness. The same region as in Fig. 1 humanized by the biotechnic "invention" of sedentariness: conscious identification of the community with its land.

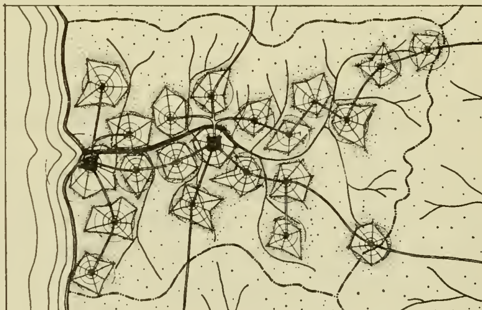


Fig. 3. Urbanity. The pattern of rural-urban regional environment: a new social, biological and environmental adaptation of society to the characteristics of a watershed basin; the coexistence of a variety of elements in a unified regional framework.

(*Drawings by Mrs. Alina Yaron*).

the faculty of organization of biotic processes. Man creates an artificial landscape, in which fertility and water are preserved by actively fulfilling the rule of return observed in nature. The disturbed cycles of growth are ever-restored by transportation, storage and the use of seed, fertilizers, water, crops and materials. This requires a continual investment of human and material energy to maintain the artifact, implying far-reaching environmental change. By this achievement, man necessarily alienates himself from the ecological context; but he uses his new position to establish a relationship to the land on a new level. On this basis mountains are shaped into cultivated step-pyramids and valleys are converted by irrigation into huge containers and renewers of fertility. The earlier instinctive integration of hunters and collectors in the natural space and time is developed into the active identification of farming communities with their environment. Land becomes a community's own ground, while a community belongs to a specific landscape. Inter-communal contacts are characterized by whether they occur on one's "own" or "foreign" territory. Man assumes a central position both in the eco-system and—physically—on his land. The new order embodies the creation of a concentric environmental system, consisting of a nucleus—the place of human habitation, storage, processing and community life—and of peripheral areas of use of land, water, forest, serving a different frequency of human movement and a different intensity of land use.

Human mobility is now essentially confined within the village lands. It assumes the form of a radial flow of men, commodities and energy from the centre to the periphery and back. Within this space man cuts down most of the natural vegetation and replaces it by species which support the qualitative and quantitative increase of his own kind. But the maintenance of this artificial environment and its defence against the return of natural vegetation call for such constant human attention that man becomes inseparable from the very vegetative process he introduced. His life now bears the characteristics of being both animal-mobile and vegetative-stationary.

By cultivation man shortens the time which a natural recuperation of fertility would require. This intensification makes possible a considerable increase in the size of concentrated communities and of population density in general. But sedentariness also means man's increased vulnerability to seasonal changes of climate, floods and drought. To meet these dangers, and to create a bearable domestic micro-climate throughout the year, permanent houses are built and grouped in village clusters. But the characteristic determinant of environmental structure is the organization of biotic processes (Fig. 2).

Urbanity

Town building represents an additional artificial arrangement in the human environment. Since the land can be made to produce more food than is required by the primary producer for his own and his family's needs, it can also supply a "surplus" urban population with other aims than land cultivation. In principle these aims are social: the creation of a new ecological system of social interaction, of classes and professions, in which the farming population is only one layer, though the basic one. The urban population considers itself as living no longer from the land, but by the mutual exchange of goods and services among men. The individual now belongs not to a particular landscape but to a social organization spread over a whole region, which may contain villages, hamlets, forests, water resources, etc., and at least one fortified urban nucleus. This centre absorbs a major part of the region's products, and from it the region is ruled. The human determinants of land use are a sociological order on the one hand and an agricultural order on the other hand. Where these orders exist in mutual harmony, men find their living space extended over a whole region. The radius of human mobility and contacts increases enormously, and the order of rest and movement changes in character. The market appears as a central focus of exchange; land use, even in far-away villages, may become more specialized, or more adapted to the natural character of the land. The urban

cross-roads are the main points of regional and inter-regional meetings (Fig. 3).

Ancient trends towards a more complex settlement structure and trends towards a greater mobility imparting a greater degree of independence of the land are integrated in the town. The town develops into an organ of country-wide and world-wide material and cultural contacts. A new dimension is added to man's environment. With communications on a world scale, many towns may acquire wider super-regional economic, social and cultural functions. Potentially there are no limits to urban growth. A professionally and culturally diversified town is essential to provide a sound basis for regional coexistence. This fact finds expression in the greatly diversified physical structure of towns, differing in principle from the village structure, which consists of groups of equal cells, the farmsteads.

Space in the rural-urban regional environment is converted partly into an interior and partly into exterior space. Arrival and departure become important objects of environmental experience and creation. In order to communicate visually and audibly with the region, urban centres rise in height and towns become three-dimensional regional objects.

The artificial social structure of the region becomes somewhat analogous to the principles of biotic structure, for in both cases the stability of the structure is safeguarded in the complexity of its composition by characteristic kinds and numbers of population. Equally noteworthy is the fact that in many cases the combination of sedentariness with non-agricultural settlement, both man-made situations, results in a new adaptation of the human environment to a natural regional framework, namely the watershed-basins. But at the same time, life in the new environmental structure becomes a matter of precarious balance. Only a step divides urban-rural mutuality from exploitation, surplus productivity from soil-exhaustion, inter-regional contacts from wars, the function of the town as a co-ordinating and distributing organ from that of a parasite.

EVOLUTION OF ENVIRONMENTAL VALUES

The ecological integration in the primordial landscape and the time use of the early hunters and collectors form a human trend which can never be lost. It reappears in most sedentary cultures, in the desire for contact with new ecological life-systems, in landscape exploration and later in the ideals of "a return to nature", and in the recreational aims of recovering the sensation of life and mobility in undisturbed nature.

Sedentariness is a cultural achievement, not because it ends the more animal and mobile kind of life and replaces it by another, but because it succeeds in uniting the animal and vegetative trends of environmental relationship in a new spatial order of rest and movement, and because it combines land use with time use in a new pattern of human life. One of the contributions of sedentariness to the quality of man's relationship to environment is that man can identify himself with an environment by feeling that he belongs to it, and by being aware of his obligation to maintain it. It is a central motif of the man-environment relationship, which we shall always endeavour to recover in some form in the course of environmental modification.

The town is a superior human environment, because—or rather, if—it constitutes a place and organ of inter-communal unity and cultural continuity. In it, mobility and sedentariness, biological and social systems, poor and rich regions, the various cultures, the individual and the community, the past and the present, all come in contact, coexist and further each other, without losing their identity. This function has been most thoroughly elucidated in Lewis Mumford's *The City in History*. Today, in regional planning, we regard the quality of an integrated urban-rural region as an ideal to be regained in the improved environment of densely populated regions, though we cannot restore it in its past forms.

The sequence of these stages, and of others not mentioned here, constitutes what may justly be called "environmental evolution". The human environment is an organization of relationships and facts, but the evolution of this organization

is in essential ways analogous to the processes of biological evolution. This evolution may be understood as the continual grafting of new types of environmental relationships on earlier types. It is not a disconnected sequence of incompatible attitudes displacing one another. At each stage specific values have been created and, in the sequence of stages, an accumulation and integration of these values has been accomplished. In this way, the reality of the man-environment relationship has been progressively extended and intensified, and so has the scope of environmental problems to be solved by man. Evolutionary continuity creates multiplicity, and integration becomes a recurring task for each new generation.

How has this "grafting" of the values of environmental relationship been accomplished? Carl Sauer gives a plausible explanation of the processes of cultural and environmental transformation. According to him, the Palaeolithic, Mesolithic and Neolithic represent a sequence of cultural stages through the integration of diversified skills and ideas originating in different regions. He considers that hunting, plant cultivation and the keeping of domestic animals were introduced to Europe, for instance, by outside people. Most cultural trends have specific "hearths" or points of origin. Environmental evolution and the related human evolution have been connected from the beginning with world-wide human interaction and cross-fertilization of diversified ideas and values. The process consists largely of the assimilation and integration of "transported" practices, attitudes and values into existing relationships, with the result that a new type of environmental relationship and structure is formed. Today, with the dispersal of technology and civilization from two or three world centres, we observe such processes in all parts of the world, but they are of ancient origin.

I have offered a few representative illustrations of the growth of man's multiple relationships to his environment and of the progressive increase of the complexity of the environment as a fact in human life. They suffice to imply three fundamental values which must be aimed at in any attempt at the creative

modification of the environment, and which have been valid since the first city was founded.

(1) The establishment of life-enriching contacts with places and communities through an order of mobility.

(2) The self-identification of man and community with a modified space and biota, to be achieved by a conscious relationship to environment, which can be realized only in an order of sedentariness.

(3) The co-ordination and mutual adjustment of human and material opposites and diversified ways of living in composite environmental structures, the towns and urban regions.

ENVIRONMENT OF METROPOLITAN CIVILIZATION

In view of these values, examination of contemporary trends reveals the extent of the present human and environmental emergency. Our answer to the problem of increased land requirements for habitation, production, circulation and recreation has been the specialization of land use, mainly in the highly developed countries. But, while the specialization of land use for crafts, trades, crops, etc., on the small scale of medieval and renaissance towns became an asset to environmental utility and beauty, a specialization on the huge scale of contemporary population concentrations disrupts the relationships of a community to the regional environment. The landscape has been subdivided into mutually exclusive or conflicting land use areas for the production of maximal amounts of food, timber, water and energy to supply the increased concentrations of population and the increased requirements of a high technological standard. The necessity to introduce new land-use types and methods has led to the implementation of powerful and quickly superseded stop-gap measures provided by science and technology. The new type of land use has not led to a new relationship, but only to an increasing alienation of man from his environment. In many regions today, "landscape" does not mean a complex biotic and spatial fact, surrounding and accompanying man's daily movements, but only an illusory notion of a recreational environment.

To connect specialized areas of land use and production with marketing and transportation centres and with the comparatively small number of great urban population concentrations, the net of country- and world-wide communications has spread enormously. But the contacts thus established with communities and landscape have led to crude colonial and commercial exploitation of population and land. Economic inequalities between industrialized and colonial or developing regions have increased and must increase further, as long as these world-wide relations are controlled merely by the free play of market forces. Technology and international communications have spread only the meanest cultural achievements uniformly over the whole world. Equally, the increase of mobility has not led to increased contact with and access to landscape and towns. So far, the space crossed by transportation is not considered and treated as a new field of human experience, but as a vacuum or an obstacle to be bridged by streamlined channels of mechanized movement, planned with the single aim of connecting several focal points of interest.

Some metropolitan centres have become, to an unprecedented degree, the meeting grounds of populations, products, cultures, knowledge and materials from all over the world. In principle this meeting of opposites might breed a new cultural integration and an enrichment of life. In the contemporary metropolis it leads to fighting among groups and individuals to the extinction of less resistant elements. It does not necessarily appear as physical murder; but increasing uniformity and mechanization bring about the same result in respect to the quality of life, the annihilation of social and environmental complexity. Uniform housing and town extensions designed for the fictitious "average" family and citizen turn urban conglomerations into "anti-town". They contradict the *raison d'être* of urban life, the co-existence and co-relation of diversified elements.

Fortunately, however, metropolitan mechanization is far from achieving its end, and we have the more hopeful condition of metropolitan chaos. The almost complete confusion and interference of all kinds of movement with all kinds of rest in

the central areas contrasts with the urban periphery where the growth of suburbia represents an attempt to escape from both the problems and the idea of the city The enormous confluence of human life and interest in the metropolitan city has resulted in self-destructive building densities, and haphazard overlapping and mutual hampering of areas of habitation, industry, business, storage, recreation and education. The private car has expelled civic life from its natural centres and from many residential and recreational areas. Unsolved traffic problems are only a physical expression of the confusion ruling all human communication and interaction in the metropolis and even in smaller towns.

As the urban environment becomes a dangerous nuisance, the same civilization provides the individual with protection from direct social and environmental contact by means of telecommunication, drugs, and the provision of an illusory environment through illustrated papers, the cinema and television. Technology is thus used to prevent, sterilize or substitute direct contact. Technological inventiveness in itself is not the disturbing factor in metropolitan life, but its use, first for raising environmental fears, then for creating protective measures which wreck vital relationships of man to environment. Finally the escape of the metropolitan population to the natural or historic environment is being progressively cut off by the commercialization of recreation or by the recreational mass-movement itself, defeating its own purpose. Only the richest classes—and outsiders—can afford to get away far enough from the great concentrations of population, and then only so long as their number is small.

Huge quantities of human work, materials and energy from all over the world are invested to maintain life in the highly developed urban centres of the world. This environmental over-development must be put in the context of the under-development of urban agglomerations in Asia, Africa and South America; there the economic surplus and technological stop-gap measures are not available, and therefore an even graver crisis of environment incompatibilities has developed. The number

of people living under intolerable conditions of poverty and overcrowding in these few overgrown shanty-towns is steadily increasing with the influx of new multitudes seeking survival. In our "One-World", these extreme contrasts of wasted wealth versus wasted humanity cannot exist concurrently for long, be it for political or moral reasons. Because of its functional inner-incompatibilities and the absurdity of its relation to world problems, we must assume that the metropolis in its present form will prove to be a short-lived phenomenon. Its breakdown would have decisive effects on the vast regions which depend in some form on metropolitan centres. The future of big cities and their regions of influence has therefore become a problem of critical urgency. The relationship of the metropolitan inhabitants to their environment has taken on an "explosive" character. A revolutionary attitude is essential.

In vast areas of the world, man has become a pathogen, a disease of nature, and there is a high degree of probability that, as Marston Bates says, "when the host dies . . . so does the pathogen".

AIMS OF ENVIRONMENTAL RENEWAL

It is an open question whether our period will be able to add anything new to the general aims of environmental relationship; but their recovery and adaptation would open up an entirely new and hopeful prospect for environmental renewal and human evolution. Renewal involves a readiness to respect and be formed by external biological and physical conditions. As breathing is vital to the maintenance of life, so an alternating passive-active relationship seems essential for human and environmental evolution.

In striving for such participation, our starting point should be awareness of the contemporary human situation. Of particular relevance are population increase, mechanized mass production of commodities, enhanced mobility, the meeting of divergent cultures, and the world-wide interrelation of human and environmental problems. Under these conditions, the achievement of the fundamental aims of the man-environment

relationship constitutes at once an enormous difficulty and a unique human opportunity.

It has been argued that such conditions determine the future of man and environment. But I believe that they are entirely "neutral" facts, and that the quality and direction of human action will determine whether, and to what degree, they will effect even greater environmental disaster or a renewal and enhancement of "environmental breathing". World-wide human contacts are potentially a means to individual and communal enrichment of life; we have reached a state in which the old ideal of the unity of mankind can be made a reality. This unity should lead to the introduction of new influences and forms in environmental creation, even on the local level of planning new towns and villages, matched with the preservation of individual and regional identity. Population increase offers a chance to intensify land use and settlement, to build better towns and villages with the purpose of enhancing the identification of man with the environment. Mass mobility makes it possible to belong to a particular place yet to enter into direct contacts with a world-wide environment and with other populations. The technology of telecommunication and transportation can be applied to the desirable location and distribution of settlements. The mechanization of production and construction should serve to meet the vastly increased requirements of population and development, and the demand to share the achievements of the world community. The meeting of cultures, economies, generations, and ideologies in all developing regions, calls for their mutual adjustment, or integration in a new composite environment.

The world-wide interrelation of environments is a new fact which has emerged in our own times. By accepting this situation, we might arrive at the formulation of a new aim for the man-environment relationship, namely continuity— meaning the world-wide spatial continuity of the humanized and natural environment as well as its temporal continuity integrating the natural and historic environment with contemporary creations.

DESIGN FOR ACTION

With our technological equipment and surplus economies, we are in a better position to tackle large-scale problems of amelioration, transportation and construction than any previous generation. But our comprehension of the biological and cultural meaning of the changes occuring in our immediate surroundings has weakened.

Experience has shown that we cannot trust the deterioration of environmental conditions in over-developed metropolitan or in poor over-populated regions to lead dialectically to a reorientation of communities. If environmental deficiencies and a hunger for a more "natural" life drive man into revolt, the result is more likely to be the total destruction of populations and culture than a search from the ground up for renewed vital contacts.

Our best chance, at the moment, seems to lie in the creation of "seeds" of future action. This is the first function of environmental planning. Designs for improvement must be ready at the moment of crisis, or, preferably, before it is reached. Environmental design is not a stop-gap measure, but the initial stage of a conscious evolutionary process. The means and ends of environmental change must be mentally and experimentally prepared by small nuclei of architects, biologists, philosophers and sociologists who have become aware of the full extent of the crisis.

Environmental modification must aim at the intensification of life, both by the strengthening of its roots through better functional arrangements, and by the elevation of the man-environment relationship to the level of a psychic experience. This integration of functional and spiritual aspects of environmental structures in a rhythmic order is the subject of art—the architectural design of buildings, settlements and regions. Architecture, thus conceived, would result from "the passage of the world into the soul of man, to suffer there a change and reappear a new and higher fact" (Emerson). Architecture creates a new level of psycho-physical relationship of man to surrounding life and space.

On such a basis, an experimental architecture might start with design for specific people in a specific environment. In the process of design, the images of environmental renewal should become suggestive of orders of rest and movement, of human "breathing" in the environment, of passages from exterior to interior space in landscapes, cities, quarters and houses. The environment should speak a "language" of contact with natural facts, social interaction and a sensible interrelatedness of the natural and the artificial components of human environment. Experimental architecture would have the pioneer function of forming both contemporary architect and architecture, of accumulating experience and of inspiring people to interest and participation in environmental change.

BEGINNINGS OF ENVIRONMENTAL RENEWAL

The conviction has grown that the scale and scope of contemporary environmental needs render reliance on trial-and-error methods of development both immoral and dangerous, and that comprehensive planning for environmental reconstruction has become imperative. The first and greatest exponent of this movement was Sir Patrick Geddes. As a biologist, geologist, sociologist, geographer and planner he conceived the full human importance of environmental renewal and of the intensification of the man-environment relationship. In spite of great building activity and a vast increase in public and private planning organizations, the realization of these ideas in our own "second industrial revolution" stands in no proportion yet to the growing emergency, the technically and economically improved conditions for large-scale development operations and the knowledge gained in planning procedure.

So much "development" is going on that it seems important to point out those beginnings which are distinctly oriented on comprehensive human-environmental renewal. First, there is progress in the planning of new urban quarters. In a number of countries the earlier monstrous uniformity of public housing is being gradually supplanted by the dual principle of "variety in unity and unity in variety", both in the social housing

programme and in the actual urban building forms. On the basis of a positive attitude towards the urban quality of living, a spatial framework for coexistence and relatedness of various human elements, has often been successfully established, at least on the level of the urban sub-unit. It is however, significant that our time has not yet produced an idea of the contemporary large city.

Of particular importance are the few realized schemes of regional planning and the influence of its ideas on other facets of planning. Regional planning is often erroneously interpreted as an attempt at artificial isolation of region-wide populations from international cultural, social and economic influences. But this is contrary to its basic conceptions and intentions. Lewis Mumford has emphasized the essential unity of regionalism and universalism. In his conception, man's relationship to environment should extend simultaneously on various environmental levels, such as the small community, the village, the town, the region, the country and the world. If one of these links is missing, the interaction between the individual and the larger communities is invalidated, and man's relationship to environment is degraded to isolation or disruption.

So far as regional planning is concerned with the renewal of a specific area, it aims at the re-establishment of human self-identification with the environment; but a regional framework of settlement, work and recreation is inherently related both to the smaller framework of local communities and to the higher level of super-regions or countries. Regional planning therefore is also a means of establishing a graduated relationship between the individual and the world.

The few existing instances of regional schemes, as in the Tennessee Valley Authority, Holland and Israel, exemplify both a trend of universal regionalism and of regional universalism. It also seems important that on the basis of this limited experience, proposals for the reconstruction of the regional landscape as the environment for both settled and mobile, rural and urban, working and resting populations have been

adopted in principle by several international organizations.

As a recent experimental step towards environmental improvement, I would like to cite a single building, an orphanage, built two years ago in Amsterdam by Aldo van Eyck. The design of this house is a result of the intellectual, ethical and artistic comprehension of the quality of movement and rest of specific people in a specific environment. The conceptual basis of the layout is, in the words of the architect, "... the reconciliation of opposites", such as the life of the individual and the collective, the experience of interior and exterior space, of lanes of movement and interaction, diversity and unity, light and shadow. These opposites are transformed into "dual-phenomena" which cannot "... be split into incompatible polarities without the halves forfeiting whatever they stand for". In the building the transitions from one particular space to another are articulated by means of "... in-between places ... providing the common ground where conflicting polarities can again become dual-phenomena". Achievements of modern building technology are applied in this house to serve its function and the development of its human qualities rather than to exhibit technology. In fact, this building, housing 125 orphans, represents a little city within a city (Amsterdam), and it is both a realization of a unique composite architectural idea and—surprisingly—of a contemporary conception of a city in a nutshell.

HUMAN IMPORTANCE OF ENVIRONMENTAL RENEWAL

Environmental renewal has a central function in the improvement of the material and spiritual condition of man. In a world of expanding physical communications, orientation on environment would present a way to a new integration, as summarized in the following points:

The environmental problem embraces the basic level of human amenity and the highest level of human evolution, its biological and cultural aspects, the individual and the collective.

The human relationship to environment is a way of establishing interaction between human and extra-human life. This

interaction is stimulated by the very expression of man's new position and function in the biosphere.

The awareness of the environment, as well as the creation of new and meaningful environmental structures, would engage and relate direct experience to science, to ethics and to art. Environmental renewal may thus become a way to fuse the separate branches of culture into a single, composite structure.

The environmental problem is in character, and today even in extent, a world-wide problem of human interaction; environmental renewal, therefore, is a means of approaching the unity of mankind on both the material and the spiritual levels.

The realization of environmental relationship is a matter of carrying the values created in past contexts into the present; environmental renewal might therefore be based upon the recognition of human continuity, and find expression in the integration of old and new values.

The mutual adjustment of opposites in a new environment, the increased material and spiritual contact among world regions, and the renewed attachment to a particular environment, might constitute the positive contents of peace.

No layout of the future world-city or of Utopia is presented here. Often the image of a progressive future is only an attempt to escape from the most decisive problems of the present. Environmental renewal is a continuous process originating in the matrix of present conditions. I have laid emphasis upon the problems of environmental values and attitudes. Once these values and attitudes are realized, environment, as a projection of an enriched human life, may assume an unforseeable multitude of functions and forms. To effect evolution instead of expecting its advent, we must reintegrate values of the man-environment relationship created in the past, to cross-fertilize contemporary cultures and to relate all of them to the present situation of man and environment.

Our concern with the fate of future generations must lead us to the intensification of our present lives. Thus man, instead of resigning himself to the tyranny of historical determinism, will impose a pattern of continuity on space and time.

Machines and Societies

D. M. MACKAY

A "MACHINE", in the classical sense of the term, represents the antithesis of all that is characteristically human. Certain functions in society—its hewing of wood and drawing of water—might be delegated to mechanical devices; but any implied resemblances between these and human agents are trivial.

The past few decades, however, have seen a radical change in our whole conception of machines and their possibilities. With the growth of the science of communication and control, the idea of a machine has been so enlarged that few, if any, specifiable characteristics are in principle outside its scope. It becomes meaningful to ask not only what function machines may perform for society, but also how far societies themselves can be regarded as machines, and whether well-tried remedies for the ills of machines can be applied to corresponding disorders of society. Since the notion of mechanism is never far from that of manipulation, this question in turn raises a crop of others which go to the roots of our traditional conceptions of social responsibility.

The present discussion accordingly falls into three parts. The first is concerned with the nature of the new scientific concepts that have so revolutionized our thinking. The second gives some examples of their relevance, both practical and theoretical, to human society and its government. In the third we take notice of some curious limitations which beset the would-be scientific investigator or manipulator of any society that includes himself.

THE SCIENCE OF COMMUNICATION

The central notion of the science of communication is that of *information-flow*. Information is said to flow from A to B when the (spatiotemporal) *form* of some happening at A determines the *form* of another at B, without necessarily supplying the *energy* for it. Thus we say that the caller who presses the front door bell-push "sends information" to the kitchen, because the form of his action has determined the form (in this case the timing) of the ringing of the bell, regardless of where the necessary energy came from.

By analysing the logical process by which a form is determined, it has proved possible to define useful numerical *measures* of "information-flow" which have given a new precision to communication science in recent years[1]; but for our present purpose it is sufficient to recognize the qualitative distinction between explanations in these terms and those in terms of traditional physics. One could say that whereas physics looks for explanations in terms of the *dependence of force upon force*, the science of communication constructs its "causal chains" out of the *dependence of form upon form*.

To the embarrassment of its practitioners, no satisfactory name has yet been devised for this new science. The term "cybernetics", coined in 1834 by André Ampère to denote the "science of government", and used by Norbert Wiener[2] to describe the science of control and communication in the animal and the machine, has recently gathered so many woolly associations that it finds limited favour.

Systems whose functioning depends on information-flow are termed "information systems". By abstracting the information-flow map of such systems we can often discern important common features in extremely diverse situations—as diverse, for example, as a self-guided missile, a human limb, and a national economy. Instead of loose appeals to analogy, it then becomes possible to apply common scientific principles in our efforts to understand or regulate these different situations.

SELF-REGULATING INFORMATION SYSTEMS

The three examples just mentioned are all of self-regulating information systems. Self-regulation of a passive sort can of course be achieved without information flow. A railway train, for example, needs no steering gear, for its course is passively regulated by the reaction of the rails. A ship, by contrast, must be actively steered according to information on its deviations from true course. To make this kind of process self-regulating (as in an automatic pilot) we require three features:

(*a*) *Control* (in this case, by the helm) whereby the form of action can be selected from a range or repertoire, without supplying all the energy required (most of which in this case comes from the engines).

(*b*) *Indication* (for example by a compass) of the deviation or mismatch between the present state of affairs and some defined goal state.

(*c*) *Calculation* of the form of controlling action which will most effectively reduce the mismatch.

In the simplest cases the third function may be performed by a direct link between indicator and control, so connected that an increase in the indication of mismatch leads to a reduction in the activity giving rise to it—an arrangement known as negative feedback. If the link were connected the wrong way round, so that an increase in mismatch led to an increase in the activity responsible, the feedback would be termed positive. Such a system would automatically drive itself so far as possible away from the goal state, becoming a goal-shunning rather than a goal-seeking system.

Unfortunately it is all too easy for a theoretically self-regulating system to become unstable, continually over-correcting itself in a growing series of wild swings in opposite directions. Sluggishness of response is the most common enemy, causing the corrective control to get out of step with the mismatch that it should reduce, so that oscillations are built up instead of being damped down. (A rough-and-ready illustration is provided by a child's swing, which is kept oscillating by suitable timing of thrusts towards its position of equilibrium.

These same thrusts, if delivered earlier in the cycle, would quickly bring it to rest.) The remedy here is to make the control respond partly to the *rate of change* of the mismatch (or even to gradient of rate of change) so as to "anticipate" the effects of sluggishness.

On the other hand, the converse fault of hypersensitivity to rapid change can equally lead to instability, and can best be corrected by artificially increasing the "inertia" of the system.

In either case, it is always possible to ease the problem by cutting down the overall sensitivity, reducing the strength of the correction evoked by a given degree of mismatch. This, however, achieves stability at the cost of a corresponding reduction in the precision of control.

Although special (so-called "linear") cases have been exhaustively treated mathematically, it is the qualitative recommendations of the theory which admit of most general application. These include (*a*) reduction of overall sensitivity to the minimum compatible with precision; (*b*) keeping the number of stages in the chain of informational control as small as possible; (*c*) making the control system sensitive to the *rates of change* of indications, and/or (conversely) to running averages, to combat respectively the effects of sluggishness or hypersensitivity to change; (*d*) arranging that any changes in the conditions against which the regulator is working (changes in supply, or demand, for example) are automatically "fed forward" to set the control roughly in the right position. This leaves only the fine adjustment to be governed by the feedback of information.

SELF-REGULATING SOCIAL MECHANISMS

Having sampled the flavour of the new mechanics of informationally-organized systems, we may find it less absurd to ask in what respects it could affect our thinking about human society. One or two examples must here suffice.

The first is drawn from the field of economics, where thinking along parallel lines was in fact initiated independently, notably by Keynes and his followers. In so far as it is possible to

abstract an information-flow model of the complex nexus by which prices, production, employment, investment and the like are interconnected in a particular society such as our own, we may expect benefits both to our understanding of present ills and to our planning of future improvements[3].

It is important to stress, however, that the safest function of such models is to suggest questions worth pursuing, rather than answers. Any manageable model is bound to over-simplify; so the process of using it should be envisaged as one of progressive refinement of the model, through the occasional discovery of unexpected answers to questions based on its present form.

Thus to an information-system theorist confronted with the instability of the old boom-slump cycle, our stock recommendations (*a*) to (*d*) (page 156) automatically suggest questions like the following: (*a*) Is any coupling or regulation tighter than it need be? (*b*) Can any stages in the chain of regulation be by-passed? (*c*) (i) Are any of the major elements known to be hypersensitive to change, or excessively sluggish? That is to say, is this instability likely to be due to too much or too little ability to respond rapidly to rapid changes? (It could, of course, have several components of either kind). (ii) If sluggishness is present, can we suitably introduce some sensitivity to the rate of change (or the acceleration) of the quantities which are fluctuating? (The precise amount and form, of course, would need to be estimated or adjusted in detail). Conversely, if "anticipatory" responses are causing instability, can we introduce some inertial factor (not necessarily at the same point) to compensate for it? (*d*) If a further reduction of overall sensitivity would at present lead to unacceptably poor regulation of the economy against the external factors that can disturb it, can we make it tolerable by introducing any sensitive devices to "feed forward" rough adjustments to our regulators, so as to compensate automatically for changes in these external factors?

Now it must be said that some—though not, I think, all—of these questions have been raised already by economists, without

recourse to cybernetic jargon. From our present standpoint this is encouraging evidence that our more general approach may be on the right lines; but even the sample list above suggests that more may yet be done to integrate economic thinking with the general theory of self-regulating mechanisms. At the least, we might hope that this would bring a deeper understanding of the regulative process in the economy as a whole. It need hardly be added that in some cases the most direct solution suggested for our ills by general theory may have no democratically acceptable embodiment! But this is a thought to which we must return.

Although we have taken economic regulation as an example, it is evident that similar questions are raised by the general theory in relation to other social information-systems such as a large business organization, or political mechanisms for the self-government of society. Here in particular we must be on the lookout for instability caused by hypersensitivity to change, since anticipation in the psychological sense can have corresponding anticipatory effects in the information-channel concerned. Whereas in economics such processes as investment in manufacturing equipment, or storage and distribution of output, contribute a certain irreducible inertia, the communication system of social attitudes and ideas has rather fewer inherently inertial channels, and many more of the anticipatory kind. The press and radio, for example, are typical channels that give preferential attention to sudden change. Since democracy is a form of social organization that relies more on self-regulation by informational feedback than any other, it is of more than usual interest to note that "improvements" in mass communications could in principle make democracy unworkable.

Have we any safeguards against this danger? Has the instability of some democratic self-regulating structures, such as that of France in the 1950's, been a case in point? Are some kinds of democratic structure more inherently vulnerable, or stable, than others? Even if such questions are already being asked with more urgency than is publicly apparent, they seem

to acquire a new cogency in the light of the facts we have considered. Even more important, the general theory does suggest definite lines along which democratically acceptable solutions could be sought without necessitating a reactionary reversal of the arrow of "progress".

DELEGATION OF REGULATIVE FUNCTION

So far we have discussed mainly the possibility of understanding existing social systems and their elements in terms of information-flow models. For many readers, however, my title may have first suggested a different question. If certain regulative social functions can be modelled in mechanical terms, can they not also be taken over by machines?

At a low enough level the possibility is now a commonplace. Not only the woodman and the watercarrier but the lift operator, the train driver, the filing clerk and even the production superintendent have already found some useful mechanical rivals. The benefits and threats of these developments to the well-being of our society have been widely discussed, notably by Norbert Wiener in *The Human Use of Human Beings*[4], and need not detain us here.

More interesting, perhaps, are the possibilities of so-called teaching machines. In principle these are no more than a way of taking a student through a book of instruction at a pace adjusted to his performance. In the more elaborate kinds the statistics of performance (right and wrong answers) are evaluated by an electronic computer and fed back to govern the programme which presents information and questions to the student.

It may justly be objected that education is much more than imparting information, so that these machines can at best be a substitute for only one of a teacher's functions. But it must be said that in this particular function they can apparently be even more successful (partly because of the individual self-pacing of the course) than many human teachers with large classes; and especially in underdeveloped areas we may expect such devices to carry an increasing share of the burden of

education, and to revolutionize the academic standards attainable with present human resources.

In science itself routine aspects of information-retrieval are rapidly passing beyond the capabilities of human librarians, and great efforts are being made to codify knowledge for machine-handling before it is too late. Here, however, we meet an interesting difficulty inherent in the labile character of science itself; for the basis of any automatic filing or retrieval system is a systematic method of determining the likely relevance of each item to others and to all possible enquiries, present and future; and it is of the essence of scientific advance that such criteria are in principle hard to find, and even harder to maintain unaltered for any length of time. It seems unlikely that any advance in machine technology can circumvent this difficulty; but since without machines the difficulty is no less and the situation even more unmanageable, the mechanization of library routine is high on the priority list at the present time.

What then of still more complex functions such as the diagnosis of disease, or the administration of justice? Both have their mechanical aspects—looking-up relevant descriptions of syndromes, or of Acts of Parliament, for example—in which something like an electronic computer might undoubtedly be used to save drudgery. Developments to this end are already under way.

Can we then expect that in due course these whole functions will be mechanized? Doctors and lawyers are not optimistic; and their most basic objection has nothing to do with any ignorance of the capacities of machines. They point out that what a patient or a litigant wants is finally a personal judgment, based partly on experience which the doctor or the judge may not be able, even in principle, to make explicit. It is not the explicit and deductive, but the implicit and creative aspects of human judgment that they believe to be irreducibly elusive of the would-be mechanizer.

Is this mere obscurantism? I do not think so. True, there now exists at least one standard procedure whereby any pattern

of behaviour that we know how to specify explicitly can in principle be mechanized (given unlimited computing capacity), using only processes now understood[5]. Thus any argument that begins "You will never get a machine to do such and such" evaporates as soon as the behaviour required is explicitly specified. What does not exist is a standard procedure for *making explicit* the behavioural specification that would satisfy us, and our fellow-citizens, in such a functionary. Even if the personal touch were to be dismissed as an optional extra, there are thus good grounds for scepticism.

I am not, of course, saying that such mechanical substitutes for human decision making will never be used. Even today millions of our contemporaries accept and even welcome the impersonal arbitrations of *Ernie* in the distribution of Premium Bonds; and to persuade such a society to accept the ministrations of some similar but more rationally disciplined ready-reckoner in matters of law, for example, might not be impossible. What I am arguing is that such a system would be fundamentally inadequate as a substitute for human judgment, and that nothing in our present stage of knowledge offers any hope that it could be otherwise.

MODELS AS PREDICTORS

Our discussion of societies as self-regulating mechanisms suggests yet another possible function for machines, as predictive models. The efficiency of government action in complex situations, for example, could be greatly increased if even a crude information-flow model were available on which to try out a change in policy. The more refined the model, presumably, the more smooth the implementation of government policy (though of this more anon).

At election time, a reliable model of voting behaviour would obviously be of supreme value to all who have the power to manipulate determining factors—unless, indeed, the possession of adequate models by all were to cancel out their value to each.

By a model in this context one means typically a large

electronic computer suitably programmed. Already such devices are in use as an aid to government in the simpler tasks of digesting massive statistics, evaluating trends and correlations, and answering specific questions, with a speed and accuracy entirely new to the art. It is certain that at present we have barely begun to exploit the potentialities of such devices as auxiliary sense organs of responsible government.

HAVE MACHINES ANY LIMITATIONS?

Is there any foreseeable limit to the competence and power of machines in these new rôles? I am not a prophet, nor the son of a prophet, and the present symposium will have its fill of prognostication. Routine aspects of information-processing in such fields as science, medicine, law, commerce, transport, and even criminal identification are obvious candidates for mechanization. Translation from one language to another may have an irreducible residue of obstacles to full automation; but no one doubts that in fields with sufficiently restricted contexts mechanical translation will eventually be with us if we want to pay for it. At present the chief benefit of research in this area has been to our understanding of the structure of language.

Electronic and other computing analogues of economic or political situations become rapidly more expensive and cumbrous as they are refined to allow for the interactions of real life; but already, as we have seen, they have thrown some light (in simple cases) on the mechanisms subserving the stability of social functions. Applications to the mechanics of business strategy and of politico-military gamesmanship are confidently proposed.

In fact, wherever the social function of human beings or groups can be reduced to a formula (if not too complex), there seems no reason to doubt that mechanistic thinking and mechanical computing devices will find increasing application.

What I want to discuss now, however, is rather the implications of such possibilities than their fulfilment. If societies are in some respects like machines, would it be possible in principle

to predict and manipulate the behaviour of societies as we can that of machines? What new kinds of responsibility have now to be recognized? And who, in this case, are "we"?

SOCIETIES AS COGNITIVE INFORMATION-SYSTEMS

There can be no question that an accurate information-flow model of a society could be a powerful tool in the hands ot anyone, in government or elsewhere, who wanted to predict or manipulate social processes to his ends. If the predictor himself were sufficiently isolated from that society, and could gain the information to keep his model up to date without significantly disturbing it, then his power might in principle seem unlimited.

Is such a society then as helpless before its predictor as a piece of clockwork? It is not, for a reason which has been hard to ignore at various points already. However mechanical may be the information-system embodied by a social structure, the significant fact is that its units are themselves cognitive information systems. This does not necessarily mean that the individual human organism, as a mechanism, is inexplicable in terms of an information-flow model. On the contrary, the logical relationship between physical, personal and even religious ways of talking about man requires no such "postulate of impotence" at the mechanical level.

What it does mean is that the behavioural characteristics of the units of a human society are sensitive to information, including information about that society, if it comes their way. A notorious current illustration of such sensitivity is the way in which the publication of an opinion poll before an election can affect people's voting behaviour, so strongly as to invalidate predictions based on it, even though the same poll, kept secret, would have given an accurate forecast. The very process of sampling public opinion can often change it significantly. The same considerations expose what Popper[6] has called the "fallacy of historicism", namely the idea that human history is inevitably predictable by extrapolation from its past, so that all a wise man need do is to discern its direction and mount

the appropriate band waggon. As Popper points out, there are many human situations where such extrapolating is logically impossible, since the attitude of the predictor himself to his prediction is one of the data needed to complete that prediction. In other words, no matter how scientific the basis of an alleged prediction of the course of history, it may still be possible for an individual or society confronted with it to make nonsense of it, by taking the opposite attitude to the one assumed when the calculation was made.

SELF-VALIDATING DESCRIPTIONS

The mechanically-minded reader may now be impatient. "Surely" he may ask "it must be possible, with a sufficiently complex predictive model, to trim the prediction in such a way that when published it ensures its own fulfilment?" There are, indeed, circumstances in which it is possible to "adjust" a poll result, for example, so that its publication brings about its own fulfilment. But in the field of human attitudes such circumstances are exceptional.

There is, moreover, an obvious objection to such a procedure at a more fundamental level. Suppose we assume that the adjusted forecast is confirmed by events, so that nobody who believed it feels himself to have been deceived. But suppose it had not been published? Then (*ex hypothesi*) the result would have been different—perhaps even reversed. Thus publication here was not primarily informative, but manipulative. And although a large computer may not always be essential to this end, the more powerful the predictive apparatus used, the more subtle and wide-ranging will be the manipulation of social attitude possible under the guise of scientific prediction.

Here, I believe, is a threat to society far more serious than any from the growth of automation. If any future use of computers wants watching on behalf of mankind, it is this; for our society's insatiable thirst for information about itself and its future has now laid it wide open to the most subtle bondage of all, in which major decisions can in principle be taken for it (wittingly or otherwise) by those whom it asks to

predict them; and in an age that takes verification as its chief criterion of truth the manipulators could have the strongest possible defence: "We were right, weren't we?"

THE LIMITS TO MACHINES AS MODELS

Behind this curious situation there is in fact a basic logical impasse. Any complete description of a cognitive information-system must include, or depend on, the information possessed by the units of the system. Any change in the information possessed by a unit must, in general, require a change in the complete description. It follows that in general, *no complete description exists which would be equally valid whether or not the units were informed of it.* In other words, no complete machine-model (nor any other complete predictive model) of a society is possible, which would be equally valid before *and* after any member of that society learned of it. In this area, then, there is a fundamental incompatibility between two of the normal aims of science—to observe facts, and to spread knowledge of those facts as widely as possible.

The implications of this could take us far afield. Here we must simply note a few consequences. In the first place, the situation of society is not quite as desperate as it might seem, for any would-be predictor of society who is sufficiently involved in that society must find his calculations frustrated by ignorance of his own (future) reactions to his own (as yet incomplete) conclusions. No improvements in his computing facilities can obviate this fundamental limitation. Moreover, even if he were to isolate himself for a time, his potential victims could indefinitely embarrass him by equipping themselves with a similar predictive model.

Secondly, on many questions of social attitude now open to scientific study, it is fallacious to suppose that there must exist *neutral* scientific knowledge to be publicly acquired. The declared aim of science is to propound conclusions which are true regardless of the attitude people take to them. It is now abundantly clear that many questions being asked of applied social science even today *have no such answers.* To recognize the

ineradicably instrumental character of public scientific enquiry here is to lay emphasis on a new dimension of the responsibility of the scientist, at present barely acknowledged. It is not simply that we are able to alter people's opinions predictably, which all propagandists can. What seems objectionable is our unrecognized and unavoidable power to do so when we are asked (and believed) to supply only "objective" information. Any situation that can give one man an effective voting power of thousands, without being held proportionately responsible, needs watching. If, as scientists, we feel it to be an undemocratic one, the remedy lies largely in our own hands.

Thirdly, this of course presses upon us the question suggested earlier. Who, in all our discussion of the matter, are "we"? We here assembled are scientists; but without intolerable hubris we cannot divorce ourselves from the very society about which we have been speaking—whose ills we would like to remedy. What differentiates us is not any special competence to decide that society should pursue one goal rather than another, but only a certain skill in calculating what may happen if it does.

Here we face a current growing point in our understanding of social phenomena. What can justifiably be believed by a group (in the first person plural) must obviously be related to what can justifiably be said by each of its members (in the first person singular). Yet as Michael Foster pointed out in the symposium[7] *Faith and Logic*, the logic of this relation (between talk of "I" and talk of "We") is still surprisingly little understood. Our present discussion has uncovered only one of its peculiarities, but it is sufficient to show the need for fresh and urgent thought on the special limitations of the scientific method and of the scientist when functioning as a guide to the evolution of social attitudes.

It is equally important, on the other hand, not to exaggerate these limitations; for great benefits, as we have seen, may be expected to accrue from a better understanding of the social mechanism. To establish that scientific investigation can only illuminate, and not replace, human valuation and commitment,

is not to belittle but to defend the proper dignity of our scientific enterprise.

What it does emphasize is the important part that extra-scientific judgments of value must inevitably play in our social applications of science. The chief object of society should be the fulfilment of the human individual—on this Sir Julian Huxley and Jesus Christ are agreed. Any disagreement must be on what constitutes fulfilment. Is it to "love God, and our neighbour as ourselves"? Or is it something else? To such questions we dare not pretend that science can give an answer; yet, as several speakers have pointed out, they are of crucial practical importance at the outset of any planning to better the lot of our fellows. To allow them to go by default, when we rightly devote so much concentrated thought to all other phases of the problem, would be to betray our calling.

My personal hope, if I may express it in conclusion, is that in years to come we shall work realistically for a more constructive relationship between scientific and religious thought on such problems. We are emerging from a period of confused conflict between "science" and "religion", revolving chiefly around what I believe were mistaken ideas of the nature and scope of both[8]. It is in a proper working partnership between the two—ideally in the same persons—that I see the best hope for the future of man.

Sociological Aspects

DISCUSSION

Bronowski: I shall confine myself to two remarks to which the three papers have prompted me.

I can best begin the first by saying that the number of fundamental particles in the universe is under some dispute, but it is supposed by some to be of the order of 10^{79} (Eddington and Whitrow). This is incomparably larger than any foreseeable human or animal population! Yet nature controls the stability of processes among fundamental particles by a very simple device: it does not attempt to manipulate them all at the same time. It builds them up into stable subunits, for instance into nuclei; then it reassembles these nuclei into more elaborate nuclei. For instance, nature takes four fundamental particles and makes a helium nucleus. Then it takes three helium nuclei and reassembles them into one carbon nucleus—the basis of all biological discussion. These nuclei are then assembled into more elaborate structures, and so on. Nature works by hierarchies. I know of no natural phenomenon which proceeds in any other way: you can only make large stable structures by building them from stable substructures. This is true of clusters of stars, say, and it is surely true of families and communities—which is the application that we are discussing now.

So I was struck in Coon's and in Glikson's talks by the recognition that whatever human community you plan, you have to start by building it from smaller self-coherent communities—sometimes from breeding groups of 300 or 400 people, sometimes from what Coon elegantly called "villages within the city".

The integration of these human groups, step by step, into national and international units has turned out to be much

more troublesome than was supposed in the time of Shelley and Godwin. But no one can doubt that this remains the only way to create large human societies that shall be stable. No one doubts, for example, that one function of a gathering like this is that we meet as colleagues and we part as friends—which is to say that we have built up new relations which we carry on into our own social groups. Therefore I take it that we can all agree that any structure of a national or supranational society that we are to build in the future will be achieved not by uniformity, but by the integration of varied and individual groups.

The second point that I want to make is that today the size of these groups need no longer be dictated by their geographical location. Technology now makes it possible for different community groups to live in small units and at quite large distances apart, yet still to make up a coherent society. MacKay's paper reminds us that modern communication makes it possible for social groups to span geographical distances—as a meeting of this kind does, for example.

I find this particularly important, because I believe that the major achievements of civilization have been created in city communities. As Glikson said, the best balance of mobility against sedentariness is struck in an essentially urban civilization. True, the world is full of academic admirers of primitive art who affect to despise city civilization; yet I notice that they continue to lecture to their students about Shakespeare, Leonardo da Vinci and Sophocles—none of whom was born in the bush. In my view, the only disaster in urban civilization has been to produce the enormous wens such as London, New York and Tokyo; however, they have now outlived their technological usefulness, in my opinion. The crowded cities were appropriate to the time of the penny post and the first railway engines, but they have no purpose in the modern age of communication. Today a community of 30,000–60,000 people can have the industries and the goods, the libraries and the concerts, and all the sense of being part of a larger concourse, which only giant cities had in the past. There is no good reason today why people should live in Sheffield in order

to make steel, or go to Manchester in order to hear the Hallé Orchestra. We can multiply these examples, both on the industrial and on the cultural level, many times over. The wide availability of energy, the growth of automation, and the biological revolution in health, are three grounds why, in the next 50 to 100 years, isolated communities of 30,000–60,000 can be just as viable, and just as cultured, as any giant city of the past. Therefore it becomes possible in the future to visualize highly integrated national and supranational bodies which are not dependent on crowded and sprawling cities for their industrial and intellectual leadership.

Price: Having been earlier somewhat consoled, pacified and encouraged by finding that the problem of man's biological habitat is not really so terribly severe, that we are likely to last for another 35 or 50 years without any hardship for about 20 per cent or so of the population, I am now extremely worried by the discussion on the sociological habitat. I am perturbed and frightened by what seems to be a traditional underplaying of this situation. Can I point out that this sociological habitat, by virtue of science and technology, is now exploding very much more rapidly than the population? The population is doubling every 35 years or so. Science and technology, in terms of manpower and publications, are doubling every ten years, that is to say, they are running through an order of magnitude, a factor of ten, with each successive generation. In terms of money, the investment in science is going up roughly as the square of the number of people engaged in it—and this is even worse because it implies doubling every five years. Science and technology, and our economic and political systems built upon them, seem to be in danger of starvation of money and people, and subject to the failure of communication between intellects. This starvation seems likely to occur within as many decades as it is going to take generations to produce similar problems in the biological habitat of man.

Can we pinpoint some of the results of this explosion of science and technology? We have discussed only the static influences on our society. Let us consider the dynamic ones, of what is

happening with the saturation of our civilization by science. We are witnessing the formation of a new élite of scientists. Having started with numbers of the order of one person per thousand being members of an élite in the early civilizations, we now, by virtue of urbanization, have a situation where the cities are so enormous and the élite is so huge that we can get an "élite of the élite". This produces a whole new machinery for communication between them—by virtue of which we are all now here.

We have new problems of computing machines and their information flow, a terrible problem in so far as it is possible for this new élite to put the non-élite out of a job. We may presume that about 1 in 5 of the population may be capable of scientific work by virtue of their peculiar psychological endowment and intellect, and the other four-fifths are going to have their jobs stolen from them by the familiar processes of automation. The technology of calculation and control is rapidly changing the life of the scientist. These developments are going to have a severe effect, a traumatic effect, on the future of man within the next generation.

I want to stress the consequences of this scientific revolution which started, after all, with the sociological invention of the Royal Society. What dominated the rise of modern science so much more than the invention of any experimental technique was the invention of the method of cumulating science. Science has been doubling every ten years for the past 300 years since that invention of cumulation was made. Now there are some very interesting consequences of this. MacKay has pointed at the machines: we have previously only considered the possibility of using machines as an extension of man's brain—to do various things for which man programmes it. It happens that machines can talk to each other, they have languages much more compatible than ours and they can talk to each other very much more efficiently than we can communicate. Our communication system is a most cumbersome thing; our ears and our voice organs are probably extremely slow, compared with our brain.

There is one nice little idea which was put up about a quarter of a century ago as pure science fiction, but which now appears to me to be within the bounds of the next generation of possibility. If one could circumvent these organs of speech and hearing neurophysiologically, by arranging some sort of mechanism by which we could plug in to each other intellectually—if, for instance, one could take the people in this room and plug us in to each other so that we could think as a unity—this would be the first self-accelerating invention. One would then not only have a multiple brain, one would be free of nature's random distribution of genii. Whoever achieves this first is going to become the possessor of such a "super-genius" that he will make all other possible inventions thereafter. This is one suggestion for a technological improvement that could vastly change the future of the human race, much more than space travel!

Huxley: I would like to introduce into the discussion a point that I made in my original talk, namely, that evolution takes place by a series of steps or grades of organization, each of which seems to reach a limit in its subsequent evolution. Bronowski made a similar point, namely, that any more complex entity has to be built up out of subunits, none of which can go further unless combined with others. I think that something of this sort is happening in human life, and we are now approaching a limit to our present type of psychosocial organization. For instance, Price has made the point about the explosive overproduction of science, and the choking of scientific channels of communication.

At this moment we are at a stage when we have to make the step from our present pattern of psychosocial and scientific organization to a new one. In this connexion I was much interested by what Glikson said about "seeds of the future", and the necessity for producing concrete examples of what the future might bring, including Glikson's example of local architectural environment. If our present stage is reaching its limit, what is going to happen in the next one? I should like to come back to what was hinted at by me in my introductory

talk (and also by MacKay and Price), namely, that we are going to have many more people thrown out of work in the ordinary sense, because work is growing increasingly technological and automated. This means (among many other things) that we shall have to occupy more and more people with exploring their own inner potentialities, their inner space.

Lederberg: I think we are here to try to continue to build a science of man. I am impressed by a few quantitative considerations that we are beginning to discover which help to define man in a different context. One important fact is that you can describe man's genetic content in terms of something like 10,000 million bits of information about the choices in the construction of a nucleotide. Another number which ought to impress us is the information transfer rate of fifty bits per second which seems to characterize us as individuals. This is extremely important because it is perhaps the one quantum from which we could start to build a theory of social interaction. It would help us to define the nature of the optimum unit of social organization.

We are not thinking enough about society's communication network, yet our urgent need is to communicate with one another. Communication sets some sort of bounds to what is possible. MacKay started by saying he was going to discuss the state of the art of communication rather than speculate about it. In fact, in our present state of communication, as he promptly pointed out, any statement of the state of the art is only a speculation. We do not understand what is happening and we have not got the necessary institutions to begin to keep up with the growth of our various communities. I have become, as everyone else has, terribly alarmed by the rate of population growth which is becoming increasingly incommensurate with our capacity to communicate with one another. I am even more impressed by the explosive increase in world culture; there is certainly, as Price mentioned, a much greater increase in the number of highly literate people than there is of the population as a whole; the number of reasonably literate people is rising by a factor of 100 or 1,000 over a period of a

century as compared to a ten-fold increase in the total population. The breakdown of scientific communication is just one aspect of it.

It is clearly time that we spent more effort not only in trying to build up world society, and in defining the dynamics of politics, but simply in trying to understand the dynamics of cultural interaction in other spheres, including the institutions by which science itself is going to be able to survive. It is becoming more and more difficult for individuality of any kind to develop and to express itself, but we have somehow to learn to live within this enlarging framework. Paradoxically, to communicate with the rest of the world we must organize ourselves in some more rational way than we do at present, perhaps in some series of hierarchical institutions. We are not in very good touch with our neighbours in world science, and we are going to be further out of touch as they grow up and begin to compete with us for the opportunity of creative performance.

Comfort: Professor Coon spoke, perhaps a little apprehensively, of the tendency to arrive at a universal police state as the end-point of scientific culture. It certainly is a risk of our time, and perhaps it always has been, but I do not think we should leave it on record that a universal police state is a necessary consequence of science. Totalitarianism seems to be inimical to the continued development of science and, moreover, since psychiatry is also a science, the exposure of the psychopathological character of police states and the motives which underlie them is quite as much a consequence of science as atomic energy is. I would not like to predict that science will enable us to avoid such an outcome; perhaps the answer may be in Coon's own observation that universal education produces ten rebels for every one genius. Indeed, perhaps that is its real justification. It inculcates contra-suggestibility of the type that MacKay has mentioned and it will perhaps at least ensure that so long as there are tyrants around there may also be daggers.

That brings me to a point that Professor MacKay made—the possibility of having a computer to govern us. I wonder

whether we should assume that the machine would fulfil the real aim for which we put it there and that it would not have any psychopathology. We trust a traffic light in preference to a policeman because it never gets too big for its boots—it never wants to push people around for its own unconscious reasons. I do not know whether we can assume this could be true of all machines. Presumably if our programming of the computer did not embody any unconscious preoccupations of the kind which we as human beings have, then the machine would be free of the factors which limit our judgments. If we are going to make a machine mimic rather than better human judgment, I suppose we should have to give it an unconscious. Then it will exhibit archetypes and structural patterns of thought which might compel us to develop, as I think Koprowski once suggested, the new skill of psycho-analysis of computers!

I am not very enthusiastic about the idea of machines for a better deception of the public by the prediction of the way they may vote in certain circumstances, and I am still less enthusiastic about the possibility of plugging into each other's brains. One of the drawbacks of meetings such as this is that we tend to assemble as a gathering of speakers rather than an audience of listeners and I suspect the signal-to-noise level might be rather poor in such a system.

MacKay: At least while one was addressing an audience, one might be glad to be unplugged from the thoughts of those one is talking to! I do not really expect our thoughts to be transferable in this way, because so much brain action seems to depend on the relative timing of vast numbers of simiI-taneous signals in parallel channels.

The great thing about a human governor is that he is *answerable.* If he turns out to be a dud there is some hope of throwing him out at the next election! Whereas an expensive machine creates a vested interest.

It should not be impossible to make a machine acceptably impartial in looking up and calculating data to guide human governors; and no doubt one could be made to imitate any

specifiable features of the behaviour-pattern of a human judge. What is doubtful is whether the "judgment" so delivered would be (or should be) acceptable by a human community. I think it is of the essence of obedience to government that in some sense the governor is answerable, even if you can only curse him under your breath.

Comfort: Perhaps we could mechanize the United Nations. The trouble about reaching a decision in the United Nations is that while we are all willing to subscribe to a written programme which lays down such ideals as liberty, equality, and fraternity, no country has ever yet lived up to its constitution. If America or Russia were as good as their constitutions they would be very fine places to live in. It might be possible to persuade everybody to agree beforehand on the programming of a "United Nations computer", but they would not then be able to go back on it when their own special case was in dispute, as, of course, we always do now.

MacKay: Until somebody says "We must replace that machine . . ."!

Comfort: There would then be such an outcry that the final programme would be altered until some animals were more equal than others!

Haldane: I should like to raise three points. The first concerns Coon's remarks about fear as a basis of religion. I think that man under ordinary conditions is not frightened enough. A moderate amount of danger, in my opinion, is extremely conducive to happiness. I have seldom been as happy as I was on a quiet day in the trenches in 1915 with a 1 in 1,000 chance of getting hit. In the absence of obvious threats, we build up objects of fear. The question is, whether it is better to have hobgoblins, like our Hindu goddess Sitala, the smallpox goddess, and Mariamma, the cholera goddess, or whether to be afraid of communists or capitalists or whatever it may be. It is very fashionable now to be afraid of lethal genes for our descendants. We seem to demand some object of fear, and the type of object of fear we should prefer to have is a question which ought to be discussed. We should realize that

as we are built at present we do demand something of that sort, and if we don't have the tiger in the neighbouring jungle, or a man shooting at us, we will make something else to frighten ourselves with.

My recipe for happiness is very simple. I could not keep up with modern technology, especially electronics, so I moved to a situation where the technology is at about the same level of development as it was when I was 20 years old, and I am extremely happy and comfortable in it.

MacKay made an extraordinarily good point about the machine whose prediction affects the future. I do not believe it is an insoluble problem, but that does not mean that I have the solution to it. Bertrand Russell might; he solved the problem of what it means when someone makes a statement such as "All statements on this blackboard are untrue". That has been worrying people since the time of Epimenides the Cretan, and Russell went far towards solving it. I suspect that the problem of the machine whose decision alters the future is soluble on somewhat similar lines. It may be beyond mechanical ingenuity, but I don't think it is beyond human ingenuity.

MacKay: Russell said that sort of statement was improper—it mustn't be made. It is indeed possible for a prediction to secure its own fulfilment (unlike the Russell statement, which ensured its own falsification). Either way, I am only pointing out that publishing the statement is instrumental, rather than simply informative. Like Dr. Comfort, I am very much disturbed that we have no safeguards at the moment against a scientist, or even a pollster, equipping himself with this kind of manipulative power, and so in effect holding many votes in his own hand, without being answerable for the exercise of it.

Coon: I agree with everything Haldane said, up to a certain point. In fact I got a considerable pleasure out of combat myself, I must admit, though it was probably naughty of me to have done so. But I did not say religion was based on fear—I said fear and deprivation of interaction. It is when you have nobody to talk to, when you are left all alone, that you really

need help. Whom do you see coming out of church but old ladies whose husbands have just died?

Trowell: One of the real problems which I have seen in this rapidly developing technological and scientific age, speaking as someone who has taught medicine for some 30 years, is that we soon get out of date, *yet we remain in power.* This I think presents the world with quite a new facet of human progress.

I would also like to add, speaking now as a parson, how much I have valued the views of some of our younger colleagues: I think we may begin to see that perhaps there are certain areas of life which science cannot explore and certain value judgments which need the philosopher, or even perhaps the leaders of religion. Certainly my village congregation is not composed largely of bereaved widows!

Lederberg: I do not think the problem of MacKay's unbiased computer is soluble, but I do not think it is important either. It is impossible to say which is the truer judgment of what the prediction ought to have been, but the fact of the situation is the final result. There are innumerable variables and one of these is the prediction that was made during the course of the election. Some people, like MacKay, say that we biased the prediction and we ought to have a counter-counter-suggestion for it. I think that it is simply an unavoidable feature of social life that there are innumerable contributions to the ultimate outcome of democratic decisions.

I should like to put another question to MacKay without, I hope, obscuring my very general concurrence with his discussion. I feel rather suspicious of one kind of machine that says to another: "Well, you're doing very well, but I also have judgment and my decisions are wiser than yours. I am unable to specify to you the processes by which I reached these conclusions, but I insist that they are nevertheless right". What is the validity of an unjustifiable judgment? Agreed, it may often be uneconomical to search through all the processes in an attempt to anticipate the final judgment. For example, in order to anticipate all the possible outcomes of an automated experiment to detect life on Mars, I would have to read all that I knew about

organic chemistry or biochemistry into the programme of my computer. In theory this ought to be done, but because the results would not justify reading so much into the computer programme and building a correspondingly large machine, I therefore reserve to myself the possibility of posterior judgment as to how I would draw an inference; I could trust such a process of judgment just so far as I felt that I *could* programme it.

Huxley: Machines, so far as I know, are not able to do what many people of genius have done in making scientific discoveries, which is to arrive at the result by a process which can only be called intuition or imagination—of course superposed on a great deal of earlier study and thought. Can machines, given the necessary detailed biological information, ever grasp the complex pattern of a situation as a whole and come to a sudden intuition of the right judgment?

Lederberg: Surely you are describing your own inability to describe the machine by which one could arrive at such conclusions? What goes on inside the computer also seems to be unconscious, or intuitive, to you.

Huxley: As comes out in Hadamard's book, many have made their discoveries in this way, completely by-passing the process of logical step-by-step analysis.

Crick: It does appear that a machine could be made which would do the equivalent of intuitive thinking, but that we cannot make such a machine yet. I know that MacKay feels there are some theoretical limitations to what can be done with machines, but it is not very obvious exactly what these limitations are. Some of the more trivial objections, such as "You can't make a machine to play a better game than you yourself can", are certainly not true. You can also make a machine which will discover a theorem.

Huxley: Can you make a machine which has an affective component as well as a cognitive component?

MacKay: In answer to Dr. Lederberg, I did not say that the predictor has less right than anyone else to influence the election. I said it was wrong that he should be able to do so unrecognized, under the guise of giving *information*. In other

words society should be told that his prediction, however well-calculated, cannot state an objective "certainty", but only something whose validity depends on their attitude to it. His rôle is quite different from our normal function as scientists, where we seek to make objective predictions which stand independent of the attitude the recipient takes to them.

A second point concerns the limitation of machines. As I said before, once the kind of performance required can be completely specified, it is in theory possible to construct a machine to carry it out. Such machines may be inordinately complex, but they can be surprisingly "original"; already for example, machines have been programmed which were able to produce novel proofs of simple theorems. The difficulty arises when we ask ourselves how to *specify* a value judgment as made by a human being, as distinct from a mechanical deduction from data. How do we decide what ought to be done, as distinct from what can be done? At this stage we do not begin to know the answer. If we did, and could make explicit the behaviour pattern that would make a machine an acceptable arbiter, that limitation would disappear.

The ultimate question is this: granted that our brains are machines, is it possible for any machine to discover and embody within itself a full description of itself? I think it was von Neumann who first raised this as suggesting a likely limit to our power to synthesize human behaviour. It is not that we cannot get a machine to do anything that has been specified, but that as men ourselves, our understanding of what it is to be a man is likely to be fundamentally limited and therefore a complete specification will always elude us.

Lipmann: I have little doubt that machines will eventually be able to do everything. The problem may really be a psychological one, namely, that we do not want to be left without mystery. An unsolved complexity has a mysterious quality and after resolving it we are dismayed to find another mystery has been "lost". I think that in the working stage it might be more helpful not to assume that there will always remain a residue that we cannot understand.

MacKay: There is a misunderstanding here. I am not disputing that what is inside my skull is a machine; but I doubt whether this or any machine could embody within itself a complete description of itself.

Medawar: Are you saying that it is *logically* self-contradictory?

MacKay: Yes, it is logically self-contradictory for the same general reason that a picture cannot contain a picture of itself: it would involve an infinite regress.

Medawar: That is a good analogy, but has the proposition been demonstrated rigorously, like Gödel's theorem* ?

MacKay: I think Gödel's theorem can be regarded as a formal demonstration of this proposition as a special case. The situation where we try to introspect into what we are doing when we are judging is essentially the Gödel situation.

Lederberg: I hope we are not confusing the issue of the limits to introspective analysis with the limitations on the possibility of a computer simulation of the human brain. We are not limited to introspection to find out how the brain is put together and we are bound to discover some organizing rules to take the place of a manifold description of every neurone and its connexions.

I would readily agree that the storage capacity of my own memory could not begin to accommodate a microscopic description of its own structure, and by a consistency argument, one might *prove* its inability to map that structure on itself. This does not prevent the mapping of that structure on another computer of larger capacity—my specification is then "copy me". The aim of all this—just what the morphologists do in

*In 1931, K. Gödel in Vienna established a theorem which has been described as the most decisive result in modern mathematical logic. Broadly speaking, Gödel showed (*Monatshefte für Mathematik und Physik*, vol. 38) that any proof of the self-consistency of a logical deductive system—comprising definitions, axioms and all the theorems derived from them—would itself involve a specific contradiction within the system. That is to say, undecidable statements exist; within a given logical system certain assertions (which may even be known to be true) can be neither proved nor disproved. In particular, such a logical system can never be self-validating, in the sense that any discussion of its internal consistency must appeal to a higher context beyond the system itself.

the analysis of the brain—is to look for the generalizations that permit a humanly useful description of the brain structure.

But even this capability is even more than we need. The validation of human thought is the end result of the processing of the data. The computer that emulates the brain might perform the task as well or better with functional elements and pathways quite different in detail, still performing the comparable logical procedures.

Klein: We are carrying out an experiment in some universities of France in which we are trying to replace the examination board by mechanographic examinations. The machine will not relieve us of all our examination duties, but it may test students who pursue studies in medical schools. We can observe our own reactions as examiners to the process and the reaction of the students also, but we are faced with this question which we have just been discussing, namely, can a machine possess judgment?

In order to programme such a machine successfully, we have to work for days to find suitable questions for the mechanographic examination, but unfortunately these questions age very rapidly because we have to keep pace with the advance of medical science. This applies also to diagnostic machines. There are highly emotional reactions to these machines from both the examination board and from the students. For half the students the machine is objective; they don't perhaps realize that we have put the questions into an examination pool. The other half have doubtful feelings about this new type of examination. Our teaching is, of course, adapted to the questions which we intend to put into the pool, and conversely. The board, too, are mostly but by no means all convinced that the machine is more objective than an examiner could be. Other people object that you cannot obtain this special thing called "judgment" from a machine. The whole experiment is a preliminary one; it exemplifies the question we have been discussing, but I think it will take at least ten years to be completed, before we can know if it is workable or not.

MacKay: This is a very helpful clarification. It shows how the process of human evaluation must go into the *design* of the machine. In principle, of course, all the machine's work could be done by a human being, with paper and pencil mechanized for rapidity.

Bronowski: In my introduction I avoided the subject of machines because I was afraid that we would get involved in this kind of detail. The only really interesting machines are the great self-correcting machines of nature, such as the atomic processes in the stars. A star is a much better self-regulating machine than anything we have built. Dr. Comfort asked what protection we have against a police state. Surely our protection against any uniform state is that we know from natural processes that you cannot organize vast numbers of identical units in any other way than by a hierarchy of groups. Even a star that fails to do this blows up into a supernova, and then has to rearrange itself afresh.

I want to make a second point about machines. We have been discussing Professor MacKay's model; but this hardly deserves to be called a machine, for it is only a thermostat! It really is a trivial piece of machinery, even by comparison with a man-made computer. Yet MacKay warns us that, by its use, we may be faced with a frightening situation in which, every time he publicly predicts that I am going to vote Conservative, I will react by voting Labour. He fears that whatever his forecast is, the public will react mechanically, for example by doing the opposite. This is to suppose that the human population will be a passive subject, and even when it knows that ten times in succession it has reacted mechanically again it still goes on doing so next time. In that case, man would be the only such machine that does not correct itself! But this is quite unrealistic. All the evolutionary processes of life are self-correcting. Whatever predictive machines come to be used, men will adjust themselves to them and learn to make them part of their daily lives, just as they learned to live with the radio, the machine-gun, and the speeches of Hitler.

Finally, Gödel's theorem is not applicable to any machine complex enough to contain a random element of correction. Gödel's theorem applies only to purely deductive systems. Any machine more interesting than a thermostat, any machine with an exploratory part, or which can change its wiring at random —to any such machine, none of these restrictions apply. For goodness sake don't let us be frightened of the Almighty in the shape of a thermostat!

MacKay: My point, which I think Dr. Bronowski has missed, was indeed that society is *not* of such a kind that it can be given infallible predictions about its own activity. If the social unit whose behaviour is being predicted were to equip itself with an identical computer, for example, it could certainly be able, as Dr. Bronowski points out, to thumb its nose at the person who is trying to do the predicting.

The feedback scheme that I described (of which the thermostat is the zero-order example) is only the basic diagram for any kind of adaptive government or control. There is no doubt at all that if such a predictive model is being used and if the members of the society are unaware of this, then, as Dr. Bronowski must realize, they are much more vulnerable to manipulation than they might have supposed. It is certainly true, as my paper pointed out, that the more people were aware what the government or others were doing with computing apparatus, the less passive would they be in the hands of the manipulators.

As for his reference to Gödel's theorem, no randomizing element can remove the restriction we were discussing, which was precisely on our power to *deduce* that a specification of ourselves was adequate. I can assure Dr. Bronowski that a randomized machine would have a harder, not an easier, job to arrive at an exhaustive self-description.

Lipmann: I wonder if Bronowski is not being too optimistic in his trust that evolution is self-regulating. We are at a point of evolution where we have to be extremely careful, because we are moving into an entirely different and more precarious phase. There are societies in nature that have become fossilized

and we should be alert to the danger that our society could eventually end up that way. In contrast to the ants, man has the power to do something about it.

Klein: I should like to refer to the building up of environments, described by Glikson. This is not only a human problem but also a biological problem for any species. As von Uexküll, the German biologist, pointed out years ago, any species living in a specific habitat builds up its own environment. As human beings, we have not yet quite grasped the significance of environment proper to each species. All that Glikson said about man may be applied to animal species also.

I agree that we have to build up new cities and new environments, but this is not a very new idea; in every century there have been people trying out such plans, especially in France where town planning has often been characteristic of French civilization. In the 17th and 18th centuries there were eminent architects who planned not only cities but also complete landscapes. I think one of the most important of these was Ledoux, who built up an ideal city in the French Jura. This city was built for a salt mine, which seems surprising, but in the 18th century salt was as precious as any material in the world. It was planned as a functional city, and not only as a decorative one, and it was set in a beautiful landscape in the French Jura. Ruins of this city remain today.

Glikson: I agree that planning is not a modern invention. Perhaps the first examples of comprehensive planning are the Neolithic villages because there you find an artificial landscape created according to a plan. Modern planning has not yet created a good relationship between the timeless values of man's environmental relationship, which we are now trying to recover, and contemporary conditions of life; we have perhaps started to consider renewal of environmental quality, but we are still far from any really valuable achievements.

Brock: MacKay's paper seems to link up with the remark made by Parkes about our being obligatory extrapolationists. Is there any other method of prediction besides extrapolation? The only other method which has been referred to so far is

intuition. Is there an intuitive prediction or is all prediction dependent upon extrapolation?

MacKay: My guess is that when we make an intuitive judgment we are not in fact working without data, but are processing data in our brains in a manner which the technician would call "analogue" rather than "digital". In other words, it is more like adjusting weights in a balance than manipulating discrete counters. If intuitive judgment is at all like this, it is not surprising that we are not aware of it in the way we are of discrete thought-processes. When a medical man, for instance, declares that he is using intuitive judgment, or is basing his judgment on experience as well as on present data, it seems possible that what he is doing is to allow his past experience and present observation to mould the *weights* given to his various explicit data. The outcome of the process can therefore be more faithful to fact; but it is still a form of extrapolation.

Medawar: I think there is a danger of a mystique growing up around the process of diagnosis. I do not think there is any difference between a clinical diagnosis and any other kind of hypothesis devised by scientists, except that a diagnosis is a hypothesis relating to a particular patient on a particular occasion. There is the same element of the intuition in it as there is in any other act of hypothesis-making, and to pretend that there is something more is, I think, pure mystique.

Brock: I am in full agreement with this.

MacKay: There is one important difference between hypothesis-making in medicine and law and hypothesis-making in other sciences. Part of the data that a clinician uses is his knowledge of *what it is like to be a man.* This may be used just as rationally as other data, although it happens to be internalized and unverbalizable, whereas in most other sciences we are able to verbalize all our data. I hope nobody wants irrational mystique; but I think it is important to recognize this distinction between judgments in human affairs and hypotheses in the more exact sciences.

Medawar: Huxley claimed that no machine could really devise a hypothesis and he gave the example of a brilliant

comprehensive intuition which could tie together a whole mass of particular facts. However, he biased his own argument by considering only acceptable hypotheses and valid intuitions. In fact, most of our intuitions are invalid. As Bronowski has explained machines can devise false hypotheses or arrive at false intuitions, as we ourselves can, and to that extent machines can devise hypotheses. What a machine cannot do is to devise correct hypotheses. There is no possibility of devising a machine trained to execute the inductive logic of John Stuart Mill.

Huxley: Descriptions by mathematicians of how their discoveries have been made show that intuition does come with this extraordinary feeling of being right. This is something very different from a formal process of logical steps. Intuition may be the result of a lot of logical steps, some perhaps in the unconscious mind, but it is not reached by a deductive process.

Medawar: You guess at the hypothesis and then deduce its consequences.

Crick: The sad thing is that you can have the feeling, but it may be quite wrong!

*The Promise of Medical Science**

ALBERT SZENT-GYÖRGYI

If we symbolize human history by a line, the present is only a point which divides the past from the future. If we want to look into the future, we can do this only by studying the past and then extrapolating. The history of science is built of three periods: the science of antiquity, classical science, and modern science.

What characterized the science of antiquity, represented by the natural philosophy of Aristotle, the geometry of Euclid and the cosmology of Ptolemy, was the absolute faith in the senses and reasoning of man. There was no doubt in the minds of these philosophers that the world was really as they saw it, and that what they saw was the ultimate reality. Problems beyond their reach could be answered by a process of reasoning that was as infallible as their senses. The earth was flat, there was an "up" and "down", and around this earth revolved the sun and skies.

That great awakening of the western human mind, the Renaissance, gave rise to a new science. This was characterized by a more modest and humble attitude which recognized that neither our senses nor our reasoning are perfect. To have a better understanding of the world we have to improve our senses with instruments and support our reasoning with careful observation, measurement, experimentation and calculation. This new science, which is often called "classical", and which culminated in the work of Newton, corrected many earlier errors and extended man's world, but introduced nothing that man could not "understand", that is, correlate with some

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earlier experience. We do not know what gravitation is but "understand" that it is gravitation which holds us bound to the sun, once we are told that it is the same force which makes apples fall, which we have seen before.

The history of modern science began with two mysterious discoveries, close to the turn of the last century (1896): the discovery of X-rays and of radioactivity. Modern science disclosed the existence of an entirely different world of which man had no knowledge before, the world of quanta and wave mechanics, a world which is more real than the one we see. The one we see and live in is, more or less, but a flickering shadow. Our senses are made so as to see this shadow, to help us live through the day. If I saw the floor I stand on as it is—a vacuum with here and there an atomic nucleus in it, surrounded by clouds of electrons moving with great speed in fantastic patterns—I would be afraid to stand on it. No human experience comes to help one to understand this world disclosed by modern science, its dimensions being far beyond the limits of perception.

This explains the danger of extinction to which mankind is exposed at present, and to which we came pretty close during the Cuban crisis. Man has returned from this new world with cosmic forces in his hand which he is unable to comprehend, which he treats as if they were still his old terrestrial forces.

Chemistry has its roots in classical science. It is true that atoms and molecules are far too small to be seen by the human eye, but classical chemistry can be "understood" with our human ideas: we consider atoms as points placed at a definite distance from one another in definite patterns and we can symbolize the benzene ring with a hexagon, with atoms placed at its corners, held together by forces which we represent by single or double lines.

Biochemistry has grown up on the shoulders of this classical chemistry and we still feel at home in its dimension. A sugar molecule is still the same sugar which I may find on my breakfast table. This "classical biochemistry" is at present dominated by "molecular biochemistry", which describes the single

molecules, big or small, with the familiar ideas of shape, force, distance, charge, and the like. This classical biochemistry harvested the most wonderful triumphs. It has revealed the solid framework of life. It not only separated most of the single molecules, it was even capable of building many of them outside the living body with synthetic methods, providing medicine with a wonderful arsenal of substances, capable of improving human life by relieving a great deal of suffering. This science is still far from being exhausted and one of its greatest triumphs, only lately, was to start to break the genetic code which opens up the hope of looking deeper into ourselves, correcting short-comings, and perhaps even taking the further development of our race into our own hands.

If I may refer at this point to my own modest work, I would mention the partial isolation of three substances from the thymus gland; one of these suppresses malignant growth, another is connected with that enviable state called "youth", and the third prevents conception. The latter two may be, perhaps, hormones of the thymus gland. It is too early to say more about them, but present experience gives a ray of hope that we may get closer to the solution of three major human problems (prevention of cancer, extension of youth and dealing with over-population).

However, if we do not allow ourselves to be blinded by these successes, we can also perceive failures, which are rather disturbing. We do not know what life is but can distinguish, beyond a doubt, between a live cat and a dead one. We know life by its symptoms, like motion, reflexes or secretions. All these functions involve transduction of chemical energy into mechanical, electrical or osmotic work. We do not understand any of these processes by which mankind has known death from life since the dawn of his history. What makes this failure disturbing is that we make no real progress on this line. It looks as if biochemistry had built only a frame from which the picture is still missing.

This failure was brought home to me during the past twenty years by the failure in my own work. More than twenty years

ago I felt I had enough experience to be able to tackle a complex biological problem. I chose motion, that is, the function of muscle. My laboratory was soon able to isolate from muscle two sorts of molecules, which could be described in the language of classical chemistry, and which, if put together in the right order, formed something like an artificial muscle, which could move outside the body and could thus be analysed with the current methods. I was convinced that within a matter of weeks we would completely understand how muscle generates motion. Then I worked for twenty years without making progress. One important point I overlooked was "organization". "Organization" means that if nature puts two things together in a meaningful way, something new is generated which cannot be described, any more, in terms of the qualities of its constituents. This is true through the whole gamut of complexity, from atomic nuclei and electrons up to macromolecules or a complete individual. Nature is not additive. If this is true then the opposite is also true, and when I take two things apart I have thrown away something, something which has been the very essence of that system, of that level of organization.

I have quoted my own research to stay close to home, but once one starts on this line more questions come to one's mind. What is the meaning of the cell? Why are all higher forms of life built of such small units of approximately equal size? What is the meaning of this most basic unit of living systems? But cells are not little empty boxes. The electron microscope has revealed a wealth of structure and organization within the cell, dominated by laminar formation. What is the meaning of these lamellar formations? There is no answer to these questions. I do not mean to say that we are not approaching these problems at all. Study of the macromolecules which build these higher structures is one approach, and the laboratory of F. O. Schmitt has shown that these macromolecules have built into them a tendency to join spontaneously in a meaningful way. But this does not answer the question about the real meaning of these cellular or subcellular formations. Intermolecular forces are short-range forces and do not explain the meaning of these

extensive membranes and lamellae. And what about the cell which must have its very specific meaning with its millions of macromolecules put together in a very specific way? How can we proceed from the molecular dimensions to the higher sub-cellular and cellular dimensions? We have to go even higher than the cell and ask: how can we explain the interaction of the various parts of the brain, this interaction which generates the highest of all functions which express themselves in psychic phenomena, as conscience, memory, recall and learning? There is still a wide gulf somewhere which separates us from a deeper understanding of the real meaning of the word "life", and a gulf which also separates molecules from higher structures.

It may sound presumptuous, but I think I can answer this question. In our analysis we have to descend one dimension deeper, below the atomic or molecular dimension, into the dimension of elementary particles, the dimension of electrons and quanta, that is, approach our problems with the mysterious ideas of modern physics. Physics has shown us that by descending into the world of the smallest particles, into the world of electrons, we can understand properties of extensive systems, like copper wires which may transmit a message from one shore of the Atlantic to the other. On this submolecular level, molecules may enter into entirely new relations which cannot be expressed in terms of chemistry and are covered only by what is called "solid state physics", which considers atoms or molecules as structures formed by atomic nuclei and surrounded by electronic clouds of fantastic and changing shapes which may fuse over long distances, in obedience to the laws of wave mechanics.

I expect the next forward thrust, in the near future, from the penetration of wave mechanics and solid state physics into biology and medicine. Such a move may enable us to give a deeper sense to the structure of macromolecules and to connect them into meaningful microscopic or macroscopic formations. It may enable us to see, in a new light, what energy means for the living organism and what the mysterious "living state" is. Mathematics has already supplied approximative methods for

the calculation of the various electronic indices, and electron spin resonance and nuclear resonance spectroscopy, in a way, enable us to see the single electrons. The beginnings are made. Suffice it to quote the magnificent work of B. and A. Pullman, who translated the chemical structures and function of a great number of biological catalysts into the language of wave mechanics, and of B. Commoner, on the electron spin signals given in photosynthesis, enzymic action and their changes in pathological conditions.

I myself have spent the last decade in trying to approach life from this end. I can sum up my first impressions simply by saying that I am frightened, for two reasons. One reason is a simple personal one. During my career I have changed trades many times, shifting from one science to the other. I did this always in the hope that I would be able to master the new principle. Now for the first time I feel that I will be unable to do so and master wave mechanics, which asks for a new breed of biologists, versed in mathematics and theoretical physics, to carry the torch of knowledge into this new dark corner.

My second reason for being frightened is more complex. If you look at the symbol of a molecule, say riboflavin, as expressed in the sign language of classical chemistry, you will see some simple geometric figures and the symbols C, N and H placed at regular intervals. It looks as simple as structures composed of the building blocks of children. If you look up riboflavin in the Pullman papers you will find the same figure but you will find a series of numbers written alongside every atom and bond. These are indices giving information about certain features of the electronic qualities. These numbers have been obtained at the price of much work and ingenuity. At the measure at which our methods improve, these numbers will become more precise and there will be more and more of them, which means that the whole molecule is not a crude structure built of elementary building blocks but a most refined and complex machine of excessive subtlety, built with a precision which far surpasses the precision of any machinery built by man. If we are ever able to find out all the qualities of

the molecule, we will probably find that this is the only molecule which can fulfil the specific function of riboflavin. This molecule has to interact with other molecules built with the same precision. Our bodies are built of thousands of such different molecules, and chains of molecules. What frightens me is the enormous complexity and precision of the system, which has now been thrown into relief for the first time by quantum mechanics. I find it difficult to believe that such an enormously complex system could have been built by blind, random mutation. My feeling is that living matter carries, in itself, a hitherto undefined principle, a tendency for perfecting itself. Whether this principle can be expressed in terms of quantum mechanics, I do not know. It is possible that we will have to wait for new physical principles to be discovered. Since living systems have arisen from inanimate ones, this self-perfecting principle may have been present already in the hydrogen atom, as the wonderful figures which the frost makes on my window in the winter are present, in a way, in every water molecule. It may be that life owes its very origin to this principle.

In reality the situation, in higher organisms, is still much more complex. What the body has to do is not simply to improve itself, but also to communicate the blueprint of this improvement to the genetic material, the deoxyribonucleic acid (DNA) of sperm and egg cells. The living organism is built from this blueprint which has to go through quite different forms of life, as shown by the butterfly which has to be, first, a fertilized egg, then a caterpillar, then a chrysalis.

And there is another astounding quality in living systems with which I am unable to cope in my thoughts: adaptability. Not only are living systems, in a way, perfect, but they are also adapted to their surroundings, and if the surroundings change, they change too. I am unable to explain this with random mutation and I believe that there must be some feedback from the periphery to the genetic material. With our present knowledge of coding and communication of the code, it is almost possible to give an acceptable theory about the mechanism of such a feedback.

One of the major difficulties of thinking about all these problems is the fact that many of the most complex structures, as, for instance, the many pathways in our brain, are built when they are not yet needed, and that the astounding potentialities of the living system are revealed only when they are called upon. A cut nerve will find its severed end; a leg, in lower animals, may be regenerated from cells which were not meant to become a leg. Cells in the plant, made to form leaves, may turn into flowers and produce seed, once they have been acted upon by hormones produced by other leaves. My brain, with a feeling of complete impotence, simply refuses to try to make a picture of the mechanism of these phenomena.

I have spoken only about the difficulties and not the promise of medicine. What I wanted to convey is that I think that we can expect three great periods in the future history of biology and medicine. The first is the continuation of the present one, that of molecular biology, which is still far from having run its course. The next great period I expect to come from the application of wave mechanics to biology. This period has already made most hopeful beginnings, but may depend, for its full development, on progress still to be made in the parent science of physics. My feeling is that beyond all this lies a third period which may depend, for its initiation, on hitherto unknown physical principles, or on a far-advanced refinement of our present knowledge, which will then open the way to the understanding of the deepest problems, the nature of life, how it originated and perfected itself.

You may feel disappointed that I have not mentioned any single lines of progress in medicine which will flow from the broadening of the foundation of biology. I give you a free hand. You may wish for anything: a cure-all for cancer, a mastery of mutation, an understanding of hormone action, or a cure for any of the diseases you have especially in mind. None of your wishes need remain unfulfilled, once we have penetrated deep enough into the foundations of life. This is the real promise of medicine.

Future of Infectious and Malignant Diseases

HILARY KOPROWSKI

Kreuzigen sollte man jeden Propheten im dreiszigsten Jahre;
Kennt er nur einmal die Welt, wird der Betrogne der Schelm.

GOETHE: *Venetianische Epigramme*

ALTHOUGH I have agreed to undertake the impossible task of summarizing the future of infectious and malignant diseases, it has become quite obvious to me that only a very perfunctory panorama of the future can be presented within the space allowed. Rather than indulge in generalities, I shall attempt to show with a few examples the problem of infectious and malignant diseases as we see them today and as we may project them into the future.

THE BATTLEFRONT

"... and I do not believe that there were any such diseases in the days of Asclepius."

PLATO: *Republic*, BOOK III

Our forebears who lived during the period of the industrial revolution witnessed the occurrence of enormous upheavals in the environment of man, which in turn made conditions ideal for the massive spread of infectious diseases. Between their time and ours the battle against diseases, carried out mainly through the correction of these upsets, resulted in the temporary arrest of the spread of many infectious diseases.

At present this spread is mainly controlled through improvements in environmental sanitary procedures such as food inspection, purification of drinking water, and the like. A minor part is played by other measures directed against specific infections, particularly those of bacterial origin.

Among these measures immunization against such diseases as tetanus and diphtheria has been effective, even though directed against intoxication and not infection by the respective agents. Antibiotic prophylaxis, directed particularly against meningococcal and beta haemolytic streptococcal infections, has also been a successful procedure in preventing these diseases; furthermore, development of drug-resistant mutants has been largely avoided when antibiotics were not used indiscriminately but were chosen because they were effective against a specific organism.

Thus the present situation on the battlefront is a sort of truce based upon the maintenance of ecological balance between man and the pathogenic bacteria. Within the conditions imposed by the truce many bacterial diseases of man are suppressed while at the same time the causative agents are allowed to propagate in nature.

FOOL'S PARADISE

> "Here, as there, exists a mob which cannot endure the thought of things to which it is not accustomed . . ."
>
> CYRANO DE BERGERAC: *Voyages to the Moon and the Sun*

There are many factors which may contribute to collapse of the truce and resumption of hostilities by the bacterial infections in the near or more distant future. Among these factors are several which even now play a definite rôle in upsetting the balance between man and his infections.

Prolongation of human life has been the goal of almost all Utopias, from Campanella's *City of the Sun* in the sixteenth century to W. H. Hudson's *Crystal Age* in the twentieth. Today, increased longevity of the population in general is no longer a figment of the imagination but a fact and also a hazard. Increased numbers of individuals reach old age, when they become a more attractive prey for infection. In addition, prolongation of life in subjects suffering from diseases such as cancer, lupus erythematosis, and others creates still another fraction of the

population highly susceptible to infections. Since people will continue to live longer and, thanks to new and better drugs, those who suffer from chronic disease will suffer longer, an increase in the spread of infections is to be expected in the future.

A more frequent manipulation of the human body, in the guise of healing, has already contributed to an increase in the rate of infections. I refer here particularly to surgical procedures which, when performed carelessly, have contributed to the increase of staphylococcal infection in hospitals. The introduction of technical improvements will lead to more frequent use of surgical procedures in general, as well as their prolongation from the present average length of one to two hours to as long as nine to twelve hours, thus also prolonging the period of exposure of the patient to infection. However, the greatest danger of upsetting the equilibrium between man and his bacteria lies in anti-bacterial drug therapy, either inadequate or based on unsound principles, and in attempts to eradicate infections.

ERADICATION OF A DISEASE—A FALLACY?

> "... non sarebbe
> qualche nuova conquesta?
> Io lo devo saper, per porla in lista."
>
> DA PONTE (Mozart: *Don Giovanni*)

In an editorial in the September, 1962 issue of the *American Review of Respiratory Diseases*, William Stead wrote the following about the future progress of eradication of tuberculosis:

> "Control of a communicable disease is usually construed to mean a reduction of incidence to a level acceptable to public health authorities. Eradication, on the other hand, entails the complete elimination of the etiologic agent from its susceptible host. The one is a relative reduction and the other an absolute elimination. Eradication requires a far greater understanding of several aspects of the disease than is presently possessed. Herein lies a great challenge for the future. It will have to be met by careful research into questions which heretofore have been viewed as "academic" or even esoteric by most people. Eradication will require a much

greater understanding of the natural history of the disease in man, the causative organisms—their mode of transmission, adaptability, mechanisms for persistence inside and outside the host—et cetera. It appears likely that eradication will depend more upon knowledge of such factors than upon proficiency in the diagnosis and therapy of individual patients with tuberculosis."

This statement can also be applied to any eradication programme planned for infections other than tuberculosis. By now it should be abundantly clear to everybody that even individual therapy rarely, if ever, "eradicates" the infectious agent from the organism of the treated individuals. If this concept is extended to the population at large, it may lead only to an alarming increase in the number of drug-resistant persisters which would be driven underground where they cannot be detected. Such micro-organisms could strike at any time and, in the absence of new and effective therapeutic measures, could cause havoc among the susceptible population.

Penicillin has been used for the rapid treatment of gonorrhoea for the past twenty years, and yet the disease has rapidly increased during the past eight years in the 12–23-year age group. Although this increase in the incidence of infection is caused chiefly by the awareness of availability of an effective therapy and a disregard for any other "safety measure", it recently became known that gonococcal infection of the female genito-urinary tract can probably never be "eradicated" even during an intensive course of individual therapy, because of changes in bacterial cell metabolism which may be responsible for relative insusceptibility to antibiotics.

Development of drug-resistant mutants has been observed repeatedly in connexion with the notorious infection by staphylococci in hospitals. Drug resistance as a function of time in tuberculosis infection has been described by Stead as follows (Fig. 1). A young adult who, let us say in 1953, showed first signs of active tuberculosis in the upper lobe of his lung in the presence of fibrotic and calcified lesions of the middle lobe representing primary infection, may have been treated inadequately. A child exposed to contact with him in 1953 would be

infected with drug-susceptible bacilli; however, if the patient's infection should become reactivated in 1955, a child exposed to him at that time might become infected with drug-resistant organisms. As happens in most cases, the primary lesions of the

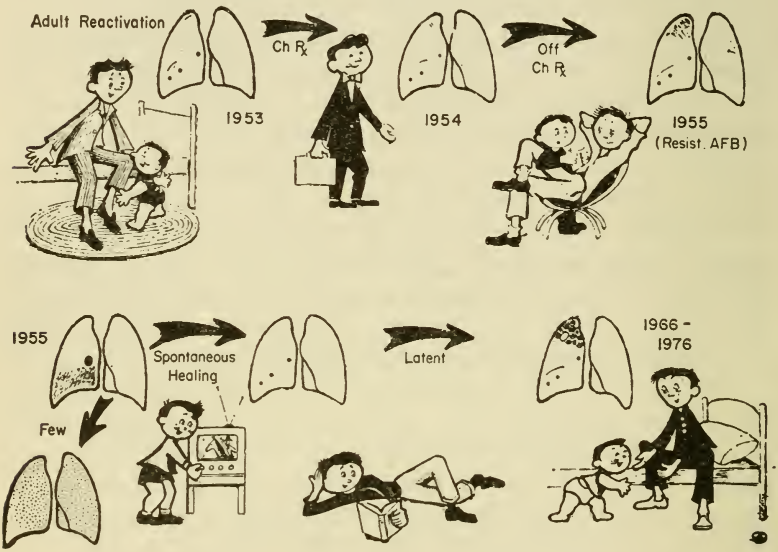

Fig. 1. "The natural history of tuberculosis: the writer's concept of a likely reason for the delay in the occurrence of resistant tubercle bacilli in untreated patients as a great clinical problem." (Reprinted with the permission of Dr. William Stead from *American Review of Respiratory Diseases*, 1962, **86**, 420.)

child will heal spontaneously; however, reactivation may occur any time from ten to twenty years later, so that drug-resistant bacilli would first be isolated in this family in the period 1966–1976. Families with a similar history are numerous throughout the world, and future attempts to control tuberculosis have a bleak outlook if drug treatment alone remains the common denominator, particularly when the initial case has transmitted the infection to contacts.

It should be mentioned in passing that a factor associated with drug resistance of some species of bacteria such as *Salmonella*

seems to have become identified with the episome, an extra-chromosomal genetic unit which may multiply independently of the chromosome or as an addition to it. This makes the factor almost invulnerable, since it can be either transmitted by conjugation or transduction or become attached to the chromosomes and associated with the genetic mechanism.

Another major danger in attempting to eradicate disease lies in the possible consequences of an upset in the ecological balance between man and his micro-organisms. The partial or total elimination of any microbial species can lead to the appearance of new, often hitherto unrecognized infectious agents which would tend, in the human body, to take the place of the bugs which had been driven out. Even now there is an increasing number of mycobacterial infections which are not true tuberculosis, and many cases of bacterial meningitis are caused by microbes which have not previously been known to play a rôle in the aetiology of the disease.

Eradication of malaria is a slogan for the immediate future; yet it has already been demonstrated that monkey malaria can be transmitted to man, and attempts at eradication of one parasite will only make possible its replacement by another which may be much harder to deal with. In general, the list of non-pathogenic organisms which may take the place of the "eradicated" pathogens in the human body is probably inexhaustible. Many of them have never been observed in connexion with a disease, and yet they may become a greater cause of alarm than the pathogenic organisms of our immediate acquaintance.

Eradication of poliomyelitis is another aim of the future public health man. What for? Even if we could not control outbreaks of polio as we do today, it should be remembered that polio is essentially a mild infection of the gastrointestinal tract which runs, in the vast majority of cases, an asymptomatic course. The virus is almost a normal inhabitant of human intestines, and its "eradication", which I hope will never take place, could lead to its replacement by other unrelated viral agents which might treat the human host much less mercifully

than polio does. (Good old polio days!) And yet an almost perfect method of prevention of polio is available for the future. I refer here, humble as I am, to the live virus vaccine, the use of which should be hailed by the slogan: "Do not eradicate, but replace." The attenuated virus substituting for the virulent one in the human gut may prevent upsets in the balance of the intestinal flora.

To place a virus *hors de combat*, anyhow, is not an easy task. Rabies is one of the oldest known diseases of mankind. Rabies virus is characterized by its infectivity for all warm-blooded animals, and the disease always ends in death. No wonder that in the course of centuries man has turned his heaviest guns against the rabies virus and, except for the folly of the Pasteur treatment, used all the weapons in his armoury in an expedient way. I refer here not only to effective mass vaccinations of domestic animals but also to other campaigns, often involving quite drastic methods such as endless quarantine, elimination of stray dogs and of wild life, and so forth. How does the virus react to such concerted attacks? Because of certain chemical components of its capsule the rabies virus can attach itself to a wide variety of receptor sites in different species and tissues. The presence of rabies in vampire bats in South and Central America has been known since the early sixteenth century. For the next four centuries the rabid vampire bats seemed to respect the southern borders of the U.S.A. However in the last decade when the public health authorities in the U.S.A. were seemingly winning the battle for control of rabies, one state (Florida) reported, in 1953, the appearance of an insect-eating bat which attacked a young boy. This bat was rabid. In 1961, 29 states reported the presence of rabid bats in their territory at one time or another. The virus played still another trick to outwit its adversary. Rabies infection was always supposedly transmitted by contact, through the "incurable wound" of Fracastorius. However, during recent years two speleologists died in the United States without apparently being exposed to the bite of an animal. Exposure of animals to inhalation of the virus from bats' excreta in the same caves led to the conclusion that

the virus had changed its ways of infecting man and that the two men died after breathing in the infectious agent.

No wonder that we do not expect ever to free ourselves from rabies in the Americas, and since bat quarantine has not yet been introduced in England, the splendid isolation (against rabies) of the United Kingdom may also end one day.

An even "lovelier" prospect is offered by a virus travelling from the animal to the plant kingdom—and perhaps having a return ticket. I refer here to the so-called reoviruses of man, which seem to be related to a wound-tumour virus of plants. Where we go from here, nobody has predicted at present.

EXTRATERRESTRIALS AND THE FUTURE

"And a man who will show every knave or fool that he thinks him such, will engage in a most ruinous war against a number much superior to those that he and his allies can bring into the field."

EARL OF CHESTERFIELD: *Letters to His Son*

Somebody looking for a needle in a haystack on the moon may not find the needle but may find *Bacillus calfactor*, a thermophilic micro-organism which is responsible for spontaneous combustion of hay on this earth. Since the earth's thermophilics are remarkably resistant to thermal damage and grow lustily at temperatures of 65–70°C for reasons not as yet clear to anybody, it is perfectly possible that moon strains of *Bacillus calfactor* or a new brand of thermophilics may withstand moon temperatures and low supplies of oxygen or none at all.

There is a biological entity on this earth called scrapie which causes a disease of the central nervous system of sheep and goats and was recently transmitted to mice. The "agent" causing scrapie can be boiled for hours and treated with high concentrations of disinfectants and antiseptic without losing its pathogenic properties.

I know nothing about extraterrestrial infections and even less about the diseases caused by these infections, but I mention the thermophilics and scrapie, since, first of all, we could send them around in outer space with the expectation that they would

easily survive to reach the other worlds, and second, some of the invading extraterrestrials may not seem as alien to us as might be expected in comparison with these two curios of our own world. This holds true only if bug life on other planets is based on a carbon and water cycle.

Future dealings with the extraterrestrials and with our own variety of microbes will depend much on the frequency and degree of stupidity among the men who will occupy themselves with these problems. If a universal antibiotic became available in the future and were used for prevention and therapy of human infections on a mass scale, a major disaster would befall the human species. There is no greater nightmare to dream about the future than the creation of a germ-free man. None other than Cyrano de Bergerac in his *Histoire Comique des Etats et Empires de la Lune et du Soleil* showed clearly the necessity of rearing man in the state of benign infection: "Perhaps our flesh, our blood and our vital principles are nothing but a texture of little animals holding together, lending us movement from their own and blindly allowing our will to drive them like a coachman, yet drive us too and all together produce that action we call life."

Germ-free animals are laboratory artifacts and anatomo-physiological anomalies which may serve a useful purpose as research tools, particularly in order to show how easy it is to upset the germ-free condition. Dubos and Schaedler indicated in 1962 that mice which have been reared free of coliform bacteria and enterococci, although not germ-free, have an abnormally reduced indigenous flora of the gut. Exposure of these mice to an antibiotic such as penicillin in the drinking water causes an explosive increase in the number of coliform bacteria and enterococci. Similar results are achieved by a single injection of endotoxin. Removal of either antibiotic or endotoxin is followed by a decrease in bacterial population.

Thus the future of infectious diseases as well as other problems of mankind will depend on the resources and ingenuity of men of the future in coping with these problems. If they understand, as many people do not, that man has to live with his infections

in a state of ecological bliss which cannot be upset by wild applications of drug therapy and attempts at eradication, then control of infectious diseases will improve even in the face of possible invasion by extraterrestrial micro-organisms.

If, on the other hand, folly prevails, man may have looked too long into the abyss and, as Nietzsche has warned, the abyss may start looking into him.

MALIGNANT DISEASES

"... because there are times when the fate of a man is not like a game of chess dependent on skill, but like a lottery."

ILYA EHRENBURG: *People and Life*, 1891–1921

It is difficult to predict the future of malignant disease because of the simple but important fact that the cause of cancer in man is essentially unknown. We may only speculate within the scope of our present knowledge on the aetiology of malignancy in general and then attempt to indicate the pathways of preventive or therapeutic approaches which appear most promising for the future.

It is quite clear that the cause of cancer is multi-factorial, and there are two principal ways in which these local clusters of fast-growing cells can acquire characteristics which enable them to become malignant.

(1) *Acquisition of malignant characteristics from within:* the cell constituents which are responsible for the specific function of the cell are changed by an event that acts upon the cell without adding a new constituent. This is illustrated in Fig. 2a, where the house at the top represents a normal organism or cell which is struck by lightning and then changes its character. Tumours caused by chemical carcinogens, physical carcinogens, and "spontaneous events" of unknown origin belong to this group.

(2) *Acquisition of tumour cell characteristics from without:* the normal cell is invaded by one or more macromolecules which alter the cell sufficiently to allow it to acquire the characteristics of a tumour. As Fig. 2b indicates the invader may be likened to a ghost which enters a house, inhabits it, and changes its character. It is clear that the "invading" macromolecules may

Fig. 2a

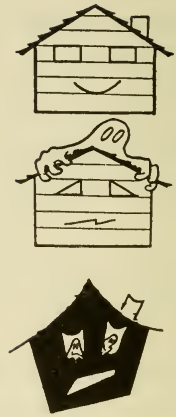

Fig. 2b

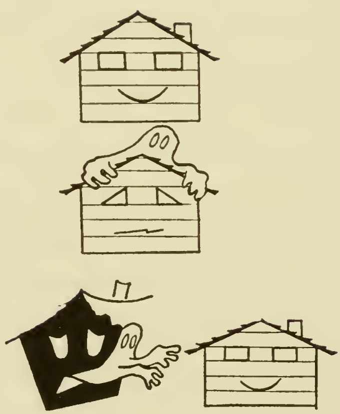

Fig. 2c

Fig. 2A. Normal cell, alteration from within and resulting autonomous cancer cell.

Fig. 2B. Normal cell, alteration from without and resulting autonomous cancer cell.

Fig. 2C. Normal cell, alteration from without and resulting dependent cancer cell.

either replace the normal cell constituents with others or add a new constituent to the pre-existing ones. Within this classification, the acquisition of tumour cell characteristics from without could be induced by the so-called tumour viruses, or their essential constituents, or by any other natural or artificial macromolecules which are able to invade a cell and function as described above.

Autonomy and dependence

Tumour cells which acquire their character from within or from without may either become autonomous or remain dependent.

(a) The autonomous cancer cells produce daughter cells regardless of repetition of the original inducing event. These daughter cells will then divide again and create a generation of cells which is essentially immortal. Most, if not all, of the tumours which acquire their character from within belong to this category. Tumour viruses which contain deoxyribonucleic acid (DNA) also seem to induce autonomous tumours.

(b) The dependent tumour cells rely on multiplication of the inducing agent in order to survive as cancer cells. Thus they may die out if they are not re-invaded by the original agent. Most, if not all, tumours caused by viruses containing ribonucleic acid (RNA) belong to this category and, as shown in Fig. 2c, the invader has to move from cell to cell since its sojourn is terminated by the destruction of its abode.

For the sake of simplicity, this description of the genesis of a malignant tumour has been restricted to these single events which actually trigger the transformation of a normal cell into a tumour cell. It is recognized, of course, that this is at most a verisimilitude of the natural event, and that many other factors have been disregarded which play a paramount rôle in carcinogenesis today or may do so tomorrow.

Prophylactic approaches

Prophylactic measures will be based upon protection against the precipitating event, when and if it is known. It is not my

wish to enter into the controversy over the rôle of tobacco smoking in carcinogenesis, but it is clear that numerous cancer-inducing environmental factors exist today and many will be discovered in the future which may be of equal or perhaps greater importance. Although removal of such factors from the environment will be one of the prophylactic measures employed, it must be recognized that it is in our power to eliminate only those factors which have caused cancer during the past few decades and not those which will cause it in the coming twenty years. Thus the success of these prophylactic measures will be significantly limited, and the generations to come will have to derive satisfaction from the knowledge that they would have been able to prevent some form of cancer in their parents, if they were still living, even though they may not be able to avoid exposure to environmental factors which might cause malignancy in themselves or their children.

Up to this year there was little chance that any procedure based on vaccination of man against a virus infection might bring about immunity against cancer, even though it had been known for some time that immunization of rodents against a tumour virus was successful in preventing growth of tumours originally induced by these viruses. However, this year evidence has been presented that three viruses, two involved in certain types of respiratory infections of man and one present in kidneys of normal monkeys, caused tumour formation in hamsters and one of these viruses transformed human cells in tissue culture. Thus it is not impossible that in the future viral agents known to cause disease of trivial nature in man may prove to be carcinogenic.

Although a direct link between these events and tumour induction in man may not be established for some time to come, the possible identification of a specific antigen in human cancer cells related in some fashion to the antigenic components of the virus or its essential constituents may raise the possibility of immunization of man against the virus and prevention of a certain type (probably only one type) of malignancy. An epidemiological study in which incidence of malignancy will be

correlated with the presence of antibodies against different viruses in a given segment of the population is an undertaking of much more heroic measure and the results of such a venture may not justify its undertaking.

Outline (for the future) of possible therapeutic approaches

The success of possible future therapeutic approaches will be related to the way in which the character of the tumour cell was acquired, and whether the tumour cell is of the autonomous or of the dependent type.

Therapeutic approaches can be divided into attempts by physical, chemical and biological means.

The physical approach is based essentially on surgical removal of the tumour or destruction of the tumour by other means. Early diagnosis and skilful surgery have been in the forefront of the therapeutic approaches to the problem of malignancy. Since it is expected that surgical techniques in the future will improve at an even more alarming rate than at present, every primary tumour growth will be accessible to total extirpation. The problems which remain will relate to the multicentric origin of the primary tumour and to metastases (secondary development). Simultaneous development of cancer cell foci in the two lungs makes the surgical approach futile. Recurrences and metastases present an even more perplexing problem, although it is quite certain that the majority of malignant cells in the circulating blood do not form metastases. Two factors which are at present under consideration are the changed state of the endothelium lining the blood vessels which permits effective passage of a metastatic cell and the possiblity that the arrested metastatic cells are genetically altered in comparison with the majority of the tumour cells and can therefore penetrate more effectively into the endothelium and resist the largely unfavourable situation of the organism *vis-à-vis* cancer cells.

Outright surgical procedures can also be applied to autonomous types of cancer which acquired their characteristics from without or from within, but in dependent types of tumours which acquired their character from without they do not make

sense, since surgery will probably serve only to disseminate the causative agent through other cells and tissues of the body. However, irradiation may find a place in the treatment of this type of cancer since it has been shown that there are periods of relatively high sensitivity to irradiation during the multiplication of ribonucleic acid viruses.

Any possible therapeutic approach based on chemical means is even more conditioned by the type of the inducing event and by the characteristics of the tumour. A highly theoretical possibility of therapy of autonomous tumours which acquired their characteristics from within lies in the neutralization of the effect of the original inducing event. This may take place by administration of an as yet undiscovered chemical mutagen for mammalian cells. Another possibility involves the use of inhibitors of the metabolic function of a cell. The difficulty here lies not in the lack of available compounds which have been successfully incorporated into the metabolism of mammalian cells, but in the ability of those compounds to reach the tumour *in situ* in unaltered form and, what is more important, to distinguish specifically and sharply between the tumour cell and the normal cell.

The use of anti-metabolites in autonomous cancer acquired from without may offer a more hopeful approach, particularly if the original event introduced a macromolecule consisting of building blocks not found in normal cells. Inhibition of metabolic functions may also lead to the destruction of dependent tumours acquired from without. The latter task will be facilitated if the attempt is directed towards the reproducing agent without concomitant damage to the uninfected cells of the host.

Future attempts at therapy of autonomous tumours acquired from within or from without based on biological approaches may include the use of "homing" devices such as cell-lysing viruses which display greater affinity for malignant cells than for normal cells. Reconstitution of normal cell functions based on the introduction into the malignant cell of normal cell constituents may also be feasible theoretically, if malignancy

depended on cessation of function of a genetic cellular constituent (minus mutation). The missing constituent could then be introduced without a carrier or by a biological entity. This is a simple procedure in bacteria; it does occur in mammalian cells grown in tissue culture; it still remains in the realm of highly unreal possibilities for tumour tissue *in situ*.

In dependent tumours acquired from without, "homing" devices are not applicable but, in addition to other biological approaches mentioned above, therapy based on irreversible binding of the inducing agent by the creation of receptor sites other than those of the host's cells may be considered.

Prevention of exposure of man to environments which may be cancer-inducing and surgery seem to be the only hopeful approaches to the control of autonomous tumours acquired from within, and I regret to say that the *negative* evidence available up to now indicates that the majority of human tumours may belong to this category. Therapeutic attempts based on chemical and biological approaches may lead to simultaneous destruction of the tumour and its host.

Although prevention of metastases and recurrences should be considered as the immediate goal of therapeutic approaches, ultimately the best, and perhaps the only, solution lies in development of recognition by the human host of the alien antigenic components of his tumour. Tumour antigens may become synthesized *de novo* as a specific protein of the malignant cells, or the antigen may reveal itself because of "inactivation" of the normal antigenic cell constituents by the malignant process. If these specific antigens were to be associated with the surface of the cell, a recognition response on the part of the host might be expected. These recognition processes would be of the utmost importance in making any other therapeutic approach successful since the ultimate destruction of remnants or recurrences of the malignant cells would become subject, in contrast to all other therapies, to a destroying force, acting specifically from within. The possibilities of attacking malignancy by stimulation of defence mechanisms more primitive than those of immunological response will be discussed below.

RESISTANCE AND SUSCEPTIBILITY

"Just as we don't know what a spirit is, so we are ignorant of what a body is: we see some of its properties; but what is the subject in which these properties reside?"

VOLTAIRE: *Philosophical Dictionary*

These forays into the future of mankind would not be complete without a brief consideration of the problem of resistance and susceptibility of man to diseases. Although Swift was sure to recognize "who first brought the pox into a noble house which hath lineally descended in scrofulous tumours to their posterity", at present, unfortunately, we know next to nothing about the genetic factors which may determine susceptibility of man to a given infection. A fairly convincing case can be built up for the relative resistance to tuberculosis of Central European Jews, who after migration to Israel about twenty years ago "mixed" with the Jewish population of North Africa and Asia Minor. The result of the contact was the appearance of a fulminant type of tuberculosis among the nomadic Jews, whereas the Central Europeans continued to suffer only from the mild variety of the disease.

More precise data are currently available about a greater susceptibility to infection and malignancy among individuals suffering from several types of congenital abnormalities. For instance, the incidence of leukaemia (of congenital type) is twenty times higher in Mongols than in normal children. Mongols and subjects suffering from agammaglobulinaemia are easy prey to infections, as are individuals suffering from other types of congenitally acquired metabolic disorders. These traits are, however, determined by sex-linked recessive genes and it is hoped they will not present any major problems for generations to come.

Whether there exists in the human population a trait which is inherited as a dominant character and which determines susceptibility or resistance to several major infections and cancer is unknown at present; moreover, it is difficult to determine which method is to be chosen to make a rational approach to the study of this important problem. For instance, we would

like to know why half the readers of this symposium will suffer from five to ten common colds during the coming year while the the other half will remain free of this affliction, even though the frequency of exposures will be the same for the two groups. We know only that this disparity in susceptibility cannot be explained by the presence of specific antibodies.

Although no approaches have so far been made to investigate this problem rationally in man, data from animals may indicate pathways to be followed in the future. It has been shown that resistance or susceptibility of mice to several infections, inherited as a dominant character, finds its expression on the cellular level in a certain fraction of a cell population known as macrophages. These cells, which are present by the million in the body of the animals, probably express the most primitive "immunological" defence system of living beings, already operative in animals on the lowest level of the vertebrate scale, such as hagfish and lampreys, which apparently cannot develop serum antibodies to an antigenic stimulus. The macrophage defence mechanism has never been adequately investigated in human subjects, particularly from the point of view of genetic mapping of man based on susceptibility of his macrophages to infectious agents. Neither has the non-homogeneous human macrophage population been divided into groups in relation to their reaction to infectious agents. Within the context of such a study, resistance and susceptibility may be discerned as genetic traits in man. Stimulation of the macrophages by certain compounds may result in cell population shifts in relation to phagocytic properties which in turn will make the host more resistant to pathogenic challenges. This has been observed in animals, which may change their resistance pattern to infections depending on the compound used and the time elapsed between its administration and the challenge. By predicting this approach, I do not mean to imply that we should revert to the application of so-called "non-specific stimulation" such as injections of milk or typhoid vaccine, methods which have been used commonly by the preceding generation and discarded as worthless. On the contrary, it is

hoped that a systematic study will lead to discovery of a variety of stimulants which would make the non-specific type of therapy or prophylaxis a specific one.

Since macrophages and possibly other cells of the lymphoid tissues obtained from mice and birds bearing chemical or virus-induced tumours were found specifically to destroy tumour cells, immunological recognition of specific tumour antigens by cells of the tumour-bearing host may take place more frequently than is suspected, but in most cases the fast-multiplying tumour cells overwhelm the defences of the host. If future generations find means to stimulate these recognition mechanisms and, *eo ipso*, slow the development of the tumour, the future prevention or cure of malignant diseases should not look so bleak.

Finally, continuing our daydreaming, if means are found to induce changes in the process of cell differentiation which favour the rise of cells capable of taking care of many common and uncommon infections, the "*milieu intérieur*" of man in the future may have a totally different aspect to the "*milieu*" of the present victims of pathogenic sabotage.

So far as a "*milieu extérieur*" is concerned, an environmental factor which plays an almost universal rôle in making man more susceptible to infection is subclinical protein malnutrition based on unbalanced composition of amino acids in the diet. As soon as this deficiency is corrected, the increased susceptibility to infection disappears. Other environmental factors such as habits, stress, climate, and protection against infection at a young age are also known to play a rôle in changing the susceptibility of man to infections. Alas, there is no indication as yet of how to change the human environment in such a way as to bring about the greatest resistance to the pathogenic challenges encountered during man's lifetime. Perhaps this task will be more successfully tackled by future generations.

LETTER TO MY GREAT GRANDSON IF HE INTENDS TO BECOME A HEALER

"It is funny, you will be dead someday."

e. e. cummings: sonnets—*actualities* II

Arcadia

Date unknown or unperceived

Dear Junior (so many times removed),

Encouraged by the inscription on old tombstones, "*Et in Arcadia ego*", I went to Arcady in order to inhabit the realm of perfect bliss and eternal happiness. Since the subtleties of the Latin language will escape you (if you ever even heard about Latin), let me tell you that I was wrong in interpreting "*Et in Arcadia ego*" as I did. It was George III of England who understood the phrase correctly when he said, "Ay, ay, death is even in Arcadia."

As you have guessed it, this is not the only time I was wrong. In order to help you avoid mistakes I have made, let me offer you a guide on problems of health which I have composed in my spare time.

1. Use computers for diagnosis of diseases which you can recognize fairly *a priori.* In cases of infections caused by agents not encountered in the textbooks of pathogenic organisms, including the extraterrestrial bugs, you may use up so much energy trying to codify the information to be fed into the computer that you may still employ the do-it-yourself kit even though it may not yet be nationalized.

2. Treat human subjects on a purely individual basis, i.e. determine the causes of the infection and the susceptibility of the agent to a given drug; use this drug alone, and use it sparingly.

3. Continue washing your hands between patients and before meals, and advise others to follow this archaic custom. I would guess that even in your time, environmental sanitation cannot be replaced by the best of the antibiotics.

4. If you happen to be a mechanical healer and if you are engaged in reconstruction of the human heart during an operation lasting for days, do not rely on drugs alone in the prevention of infection in the newly reconstructed patient. Use your brains and good techniques of sterilization.

5. Do not overvaccinate for protection against diseases. Employ only vaccines which, while protecting against one pathogen, do not spread another. Preferably, use vaccine types which will maintain the balance between infectious agents and their human host, replacing the more virulent pathogen by a more attenuated one.

6. Do not engage in programmes of eradication of infectious diseases. You will only drive the causative agents underground where they will become engaged in never-ending guerrilla warfare.

7. If a universal antibiotic is found, immediately organize societies to prevent its use. It should be dealt with as we should have treated, and did not treat, the atomic bomb. Use any feasible national and international deterrents to prevent it falling into the hands of stupid people who probably will still be in the majority in your time as they were in mine.

8. Have fun. You probably guessed from my own experience that you will never leave this world alive.

Discussions which were held with Dr. Robert Austrian, University of Pennsylvania, Dr. René Dubos, of the Rockefeller Institute, and Dr. Eberhard Wecker, of the Wistar Institute, greatly helped in formulating the ideas incorporated in this paper; the author thanks them.

Longevity of Man and his Tissues

ALEX COMFORT

THERE are two ways of considering individual longevity in prospect: we can think of what undirected primate evolution has done to longevity in the past in producing our present lifespan, and try to extrapolate what it may do in the future; or we can try to predict how we ourselves may influence human lifespan, either by our wish or by our negligence. Of these two approaches I think I prefer the second. Natural selection is bound to affect us: but Sir Julian Huxley has given us reasons for doubting whether pure first-order effects of selection pressures can ever again be separated from the mass of second-order and social effects on human biology; and in any case the principles upon which lifespans have evolved are still far from clear. No doubt they have been fixed by selection; but we have the very anomalous case of small birds, which have a standing wild mortality in the region of 60–75 per cent per annum, and a potential longevity of 20 to 30 years. This is a figure which is almost certainly never reached in the wild. We have in primates, including man, the added complications which spring from the steady prolongation of childhood and parental dependence. About this I shall have more to say when I refer to purposive attempts to alter our longevity—but for the moment it is one more reason for not offering any sweeping evolutionary predictions as to what, if anything, will happen next. Finally and most practically, if further changes take place in lifespan with further primate evolution, neither we, nor our students, nor our children, will be there to see them, whereas man-made changes, deliberate and accidental, seem very likely within the next century, and not impossible within the lifetime of some of us here present.

Contrary to what many of my own profession have believed, medicine is not increasing our lifespan, although it is making us live longer—nor is it likely to increase it in the foreseeable future by the techniques it now uses. What it is in fact doing today is to ensure that a higher and higher proportion of those who are born alive realize that lifespan. This is being done in three ways: by reducing the accidental, non-age-dependent mortality from infections and deficiencies which would kill, or shorten further life, at any age; by reducing the level of what I may call environmental attack—it is less dangerous in many ways, though not in all ways, to live in a privileged community than in an Indian village or a Neapolitan slum; and by applying specific remedies to killing diseases in later life. A law of diminishing returns operates in purely palliative life preservation, and at great ages cure of one disorder merely exposes, and sometimes aggravates, another—rather as replacement of a faulty component in an old radio may restore voltages to their correct original levels and blow out several other components which can no longer stand them. It seems quite certain that, failing a radical interference with the whole process of ageing, the prediction that medicine will give us 150 or 200-year lifespans, which was incautiously made by a number of nineteenth-century optimists, is wrong. The best we can hope from medicine and hygiene is that the histogram of lifespans will become increasingly Gaussian about a mode of, say, 75–80 years, and that its tail at early ages will shorten.

Consider first the possibility of changes due to inadvertency. Most of those which one can foresee are likely to be adverse. Man has been killing himself prematurely for a long time by social, dietary, religious and political means. In general, these mischiefs are either semi-accidental in their age distribution, or are distributed along the vigour decline like other natural hazards. When wars used to be fought preferentially by and against young adult males, instead of against women and children, this arbitrarily affected the male survival curve. Motor-bicycle-riding still does so. The hazard of smoking is very similar actuarially to many cumulative industrial hazards

—silicosis, for instance—in having a cumulative factor superimposed on an age-dependent increase. Psychosomatic stress, and particularly, it seems, the type of stress we find in prosperous modern urban communities which are anxious and bored (what I would tentatively call the Ulcer Belt Syndrome), might conceivably have a more fundamental effect on the rate of ageing, if the Pavlovians are to be believed—or it may be simply one more factor of environmental attack. But there are two cases where an adverse change in lifespan may be more fundamental: chronic over-nutrition, and radiation.

Of these two possible causes of change in the rate of natural ageing, I think the second is the more convincing. Over-eating by adults certainly shortens life, but there is probably no fundamental difference actuarially between this type of shortening and the shortening induced by malnutrition: they both represent increased environmental attack. The case for a fundamental life-shortening hinges rather on the more rapid development of modern children, and the consequent abbreviation of childhood. The age of puberty has, it is said, advanced by about four months per decade over the past century. The argument is that as the lives of rodents can be prolonged nutritionally by keeping them immature, rapid growth is likely to reduce human life by the amount that adolescence is advanced, if not by more. I do not myself find this at all convincing. Genetic sexual precocity, though it is, of course, not strictly analogous to dietetic acceleration, does not noticeably shorten life, and there is strong ground for thinking that the present trend represents not an unusual shortening of childhood, but a return to normal after an epoch of unusual retardation. I will not pursue this argument here, beyond saying that the present age of menarche in privileged countries is about what it was in Roman law[1], and in the days of the Abbé Brantôme.

One specific threat to our natural lifespan is the increasing use of ionizing radiation in medicine and industry. This is clearly the major source of extra radiation exposure today, but

the release of radiation by psychopaths in the course of bomb-testing cannot be ignored. It has so far contributed a much smaller amount than the individual dose which we receive in civilized countries with busy X-ray departments, but it may well eventually contribute more to the dose received by the human genome as a whole. We still do not know whether low-dosage radiation really accelerates ageing. It may do so, or it may only simulate an acceleration of ageing by reducing vitality in some way unrelated to the normal ageing process. If ageing is accelerated we should expect animals that die earlier than usual after low-dose irradiation to do so from approximately the same causes in approximately the same order as their unirradiated littermates. Lindop and Rotblat have recently shown that in general they do die from the same causes, but not in exactly the same order.

We do not as yet know whether the study of radiation effects will prove to be the key to the normal ageing process or simply a mischievous diversion of energy, nor is it at all clear what law of equivalence relates the life-shortening effect in rats and mice to that in larger animals and man; that is, would the equivalent dose which reduces the two-year life of a mouse by three months reduce human life by three months (which would be nearly undetectable actuarially), by a quarter, by some other amount, or not at all? A claim of a significant radiation effect on the longevity of radiologists in America has not been confirmed in a later study of English radiologists from 1897 to the present day. We have no life-tables yet for people who live in areas with a high background of radioactivity. Whether politicians have already shortened our lives by exposing us to increased background radioactivity and unanticipated local concentrations of isotopes, whether our physicians shorten them even more by the use of diagnostic X-rays, and, if so, by how much, nobody yet seems to know. Caution seems necessary, because the effects could conceivably be large, and for this reason it may be politic not to speak too loudly of any possible gain in longevity from mutation-induced heterosis in man, though that too is a possibility.

Harman in America has lately been trying to use anti-radiation drugs to reverse or delay the effects of normal ageing in mice. His results are, in my view, equivocal, but the idea is an interesting one.

It leads me to the oldest and most elusive of human ambitions. "*Ah quanta spes est lapidem sperare sapientium*" wrote[2] Kaau von Boerhaave in 1737; "what a hope that is, to have the philosophers' stone! To hold to an unfailing bodily health, a constant vigour and tranquillity of mind, to preserve these into a green and rugged old age, until without a struggle or a sickness body and soul part company: . . . nay more, to regain lost youth—the old granddam to win back a merry suppleness. . . the wrinkles of her brow to fill and level, so that she straightens and she shines . . . even old moulted fowls to feather and lay eggs again. Yet alas for that fortunate hope: the nearer they win to it, so much the more does possession threaten present dangers to them that all but have it, and how these may be avoided I do not know."

It may not, of course, prove possible to avoid them, particularly where the reversal of established senile change is concerned. Some biologists would share the pessimism recently expressed by Strehler[3], who suggests that the only unity in age effects may be what I have elsewhere called a loss of programme, due to the failure of natural selection to secure homoeostasis at great ages. Such pessimism, although it may eventually prove correct, is less in evidence now than it was ten, or even five years ago. The operational attempt to interfere in age processes is now, at least, being taken seriously by people other than quacks and the obsessed; the number of teams clocking on daily to work on the project, in the United States alone, was over 800 last year, and is going up there by about 200 a year.

What has so far been achieved in this direction? In one sense very little, certainly not enough to make it possible yet to predict either the feasibility of controlling our rate of ageing, or the pattern which such control would produce. There are still three major hypotheses of ageing in the field: that it is timed by the loss of irreplaceable cells and structures, that it results from

faulty copying in cells which divide clonally, and that it is a mechano-physical process involving the "setting" of low-turnover colloids and other macromolecules.

It would be a very brief and satisfying explanation of age changes if they were due simply to the steady loss of vital and irreplaceable cells. One difficulty in assessing this view, apart from that of counting cells, and knowing what cells to count, is that we do not know what makes fixed post-mitotic cells die, or how far their enzyme system can be damaged by events analogous to mutation. Certainly animals such as insect imagos, which have little or no cell division, are inordinately resistant to life-shortening by radiation. It may be that the rat experiments carried out by McCay, in which life was prolonged, effectively, by lengthening childhood through calorie restriction, are in a sense irrelevant to the problem of prolonging human adult vigour, for in all probability this type of manoeuvre acts by delaying development, and perhaps merely by postponing the age at which certain timekeeping cells reach their fixed post-mitotic state; and it may be that the real problem will prove to be one of conserving these cells as we conserve irreplaceable teeth—not so much of postponing the age at which the permanent set erupts, as of preventing decay and filling biochemical cavities as they develop. It would be tempting to look on loss of neurones *per se* as a possible timekeeping mechanism, for both between species and between breeds within a species it is the index of cephalization—the excess of brain over the expected amount—which is correlated most closely with longevity, and next to the biochemical information store in cell nuclei the central nervous system is our main and overriding homoeostatic system. If this were so, if the deterioration of fixed post-mitotic cells were the timing mechanism for mammalian senescence, the prospect of slowing it seems by no means hopeless, for the very diversity in the rate of ageing between similar mammalian species suggests that the rate of spoilage might be accessible. When typical ageing can be produced by experimental damage to the brain, I shall be prepared to take this particular speculation further. At the

moment, though some would locate the cause of Simmonds' disease, which has some characters of a reversible senescence, in the pituitary hypothalamic system, nobody has apparently ever produced ageing effects by giving a nerve cell poison or by experimental injury to the brain. It may be that the effects of these are too local or too widespread. And there for the moment the matter must rest.

Somatic mutation is today a more popular theory than mere loss of cells. My colleague Mr. Maynard Smith has attributed its popularity—rightly I think—to three things: the fact that mutation in clonally-dividing cells would eventually produce ageing if nothing else did, the fact that a theory which is cousin to cancer research and radiobiology is a sure grant-winner, and the fact that it lends itself to the construction of elaborate mathematical models by non-biologists. If we widen the field to include not only point mutation but all possible copying errors, including deletions, aneuploidy, cross-linking and chromosome anomalies, then this group of theories might now secure a majority vote. The majority is not always right, however. In favour of the faulty-copying hypothesis are the apparent age-accelerating effect of low doses of radiation, the recent finding that some but not all chemical mutagens shorten life in much the same way, and the appearance of several papers suggesting that aneuploidy in somatic cells increases with age. Against the hypothesis are the huge somatic mutation rate which would be required to account for the observed rate of ageing, and the fact that if point mutation were the sole process involved, the life of a haploid should be vastly inferior to that of a diploid. In amphibia this is true, but haploid amphibia are poor things, and in the gall wasp *Habrobracon* haploid and diploid males have the same order of lifespan, though the former are far more radiosensitive.

If generalized mutagenesis were the main cause of our ageing, I would feel unoptimistic about the possibility of interference with it. It need not, however, be generalized in order to be a timekeeping mechanism—if the important error were confined to one system it might well be possible to gain a few years

artificially. Burnet has recently suggested that the particular mutations responsible may be those which accumulate in lymphocytes, giving rise to clones which ignore the ban on the production of antibodies against body constituents. This hypothesis may or may not be correct, and I give it here simply as an instance of a mutative process which it might conceivably be possible to modify. A process of this sort could meet the statistical objection to point mutation as a cause of ageing by simple cell loss. Maynard Smith has computed that, given rates similar to the apparent rate of germinal mutation, about two million cells would have been affected by the age of 30, and perhaps four million by the age of 60. If loss were the cause of ageing, this is not enough. If, however, harmful properties and a selective power of clonal multiplication were also involved, the numerical possibility seems rather better. We can still hope, therefore, for a more localized and tractable cause for the rise in mortality with age than generalized somatic mutation.

The longevity of human tissues in storage is not, perhaps, likely to have a great influence on our longevity as individuals. There is the same fallacy in the conception of spare parts as a fundamental remedy for senescence as in the idea that better medical services will push up the limit of the lifespan; some of us certainly age more rapidly in one system than in another, but ageing is characteristically an increase in the number and variety of homoeostatic faults. For this reason alone the interest of grafting and storage techniques for age studies is still much more for their contribution to theory than for the chance of using them as a prosthetic remedy for ageing. Professor Krohn's work in making age chimeras by grafting mouse ovaries from old to young and from young to old is an elegant example of this kind, but it was found that a transplanted ovary did not gain in longevity from being in a young environment.

Both organ culture and organ storage might throw some light on the rôle of somatic ageing in mutation, and on the related problem of the general stability of somatic cell-clones. I must confess to being somewhat lost in the literature of tissue and

organ culture; the published claims are contradictory. There is still doubt whether any cell which is kept dividing serially in culture is really unchanged from its original genetic status—and from what one knows of hidden selection and divergence even in slowly-reproducing creatures like mice, one might expect such effects in cell cultures to be very large indeed. Probably there will prove to be some somatic cells which form stable clones and others which do not.

If somatic mutation, or any similar process based on copying faults, really does operate to time the rate of ageing, then we should find signs of it in stored and in cultured organs, unless (1) isolation leads to selective proliferation of unmutated cells, or (2) there are very big differences in the rate or the expression of the process between different organs. If Burnet is correct in his speculation about the rôle in ageing of mutated lymphocytes which have lost their inhibitions about producing autoantibodies, we might find that organs are longer-lived if they can be cultured in the absence of lymphocytes, or in the presence of hand-picked lymphocytes only. But in spite of these possibilities, the information we really need about cell longevity, individual and clonal, in order to reassess ageing is that which deals with somatic cell behaviour *in situ*. If we had comprehensive information about the life-time changes in total and in functional cell number in a sufficient range of mammals alone, we could probably reduce the factors which may time ageing to a short list without further ado.

Apart from these ideas, we are not really very much further on with the age problem than we were when the first Ciba Foundation conference on ageing[4] met here in 1955. We have collected a good many more data about ageing in vertebrates other than man. For example, it now appears likely that ageing occurs in lower vertebrates which display indeterminate growth as well as in creatures like ourselves, which have a fixed size—a point which is theoretically interesting in view of what I have been saying about the relative rôles of fixed and of dividing cells. The most striking example of an experimental prolongation of active life in mammals is still the dietary experiment of McCay

to which I have already referred, and that is now thirty years old. And yet I do feel a certain confidence that we are a good deal closer than we were to knowing whether we are likely to be able to influence human ageing in the near future. We are perhaps near enough to spend time occasionally in considering the probable consequences if we could do this, because we, or our sons, might at the very least prevent some foreseeable mistakes and abuses if, for once, we think out the possibilities of a new advance in human potentiality before it is actually upon us, and before we know whether it is practicable.

One point which is often raised when one speaks of this work, and an obvious one in the light of what we have been saying at this conference, is the relation of gerontology to the threatening growth of world population. If we could lengthen our lives, that would clearly have demographic effects which would depend on the size of the increase, and, still more from the practical point of view, upon which section of the life-cycle we are able to prolong. You may recall that Tithonus in Greek mythology induced his goddess-wife Aurora to secure him immortality from Zeus, but forgot to ask for perpetual youth. Cadmus, more wisely, opted to become an animal with a long period of adult vigour, and he and his wife were metamorphosed to "two bright and aged snakes that once were Cadmus and Harmonia". If we were to produce Tithonuses—and that, to some extent, is what medicine is doing by prolonging life after vigour has declined—we might merit the scepticism which is sometimes expressed about prolongation of life. But that is precisely what gerontology is trying to avoid. If we could prolong adult vigour with no increase, or only a small increase, in the two phases of dependency—childhood and old age—then every day of productive life gained should be a gain to humanity. At the moment we may spend from one-third to one-half of our potential life in training to become productive, whether we are farmers or biologists, and then at the height of our experience and performance we are removed by death or infirmity. Anything we can do to increase our working life

seems therefore worth doing. The other important demographic factor is whether or not our reproductive period is to be increased correspondingly. It almost certainly would be in men, and it might be in women. It has been suggested that the suppression of ovulation by Dr. Pincus's pills might have this effect in any case through ovum-sparing and the cutting down of losses from atresia. This might in turn have some unwelcome genetic effects—but it might well be that the disincentives to reproduction after the present limiting age will be strong enough to limit its demographic significance.

The most important single change in our world, where lifespan is concerned, is that in privileged countries our children grow up and reach old age and our wives no longer die in childbirth. Men have always known the probable limit of their lives. We now know more accurately than ever before when we are likely to die. The most important future change depends on the progress of our understanding of fundamental age processes. If the present trend of medicine continues without such progress, all that will happen is that the commonest age of dying will shift from being nearer 75 to being nearer 85, and the commonest causes may change so that we die of conditions which are not now so common, today's most frequent killers having been removed to uncover the next layer of the onion. If this is all, not many more than the present 2 in 100 born will reach 90, and not many more than the present 1 in 1,000 will reach 100. Those who do will still be the progeny of long-lived stocks, and owe more to their parents' genes than to medical science.

If, on the other hand, fundamental interference does become possible, so that we can modify the rate of ageing itself, the picture will be different. It might prove possible, first of all, to lengthen the period of adult vigour without increasing the final lifespan. This would produce a nearly square survival curve with its limit short of the century, and a situation like that in Aldous Huxley's *Brave New World*, where people remained apparently young until great ages and then died suddenly at approximately the usual time. This seems biologically the least

likely pattern for us to achieve. More probably we might find means of prolonging the period of adult vigour, either alone, or with proportional prolongation of the pre-adult and the senile stages—a scalar expansion of our present survival pattern. Finally, and perhaps least profitably it might be possible to prolong the total duration of life only by prolonging the stages prior to maturity. This seems to be the nature of the effect observed in the rats McCay used. Its utility in man would depend entirely on how late in the process of development it could be made to operate. There would be little point in interpolating five or ten years at a physical and mental age of twelve, except perhaps to make a longer period of pre-adult training possible. If there were any way of stopping or slowing the clock at a later age, that would represent a more significant achievement—a marking-time for, say, five years at the apparent age of twenty or thirty, after which bonus we should complete a normal life-cycle. Of all the possible modifications which the system childhood-adulthood-senescence could undergo, this comes nearest to the aims of von Boerhaave's alchemist, leaving aside the reversal of established senility, and it seems the most socially desirable. At the moment it is possible to produce this result experimentally in fish, which respond to dietary retardation not by remaining immature but by failing to increase in size. Or the rate of scientific progress in the prolongation of life might conceivably become such that provided one was young enough for treatment, one might hope for a series of such bonuses, as many patients with incurable diseases today have some reason to expect that the rate of progress in medicine may be quick enough to save them. There is only one reason for mentioning this possibility, and that is this: the psychological effect of anything which rendered the prospect of individual survival "open ended", even if the real gain in years were not great, could, I think, be extremely profound. The knowledge of our fixed lifespan—an idea we verbalize quite freely but do not usually admit fully to consciousness—may well play a much bigger part in our emotional life than we realize; it is one of the earliest unpleasant intellectual discoveries which

we make. If we lost it, it would alter both us and our culture.

It would be typical of the trend of science generally if we did bring this about, for science characteristically reduces the number of physical necessities and emotional certainties, thereby increasing the range of human choice. Whether it can do this to the lifespan, by freeing us from the necessity of becoming infirm and dying at the fixed ages we now must, remains to be seen.

Health and Disease

DISCUSSION

Medawar: I would like to thank the three speakers for being so amusing and pointed and cogent. Their papers were so full of combustible material that it is hardly necessary to open the discussion. I had one general reflection on Dr. Koprowski's talk: we speak figuratively about the advancing front of medicine, but in point of fact there is no such thing. Medicine has no one front and it does not move forward as a whole. In the study of infectious diseases in advanced countries, I think it is true to say that the major task of medicine has already been accomplished. The force of mortality cannot fall below zero and the asymptotic character of its approach to zero is already perfectly obvious, anyhow up to, say, the fiftieth or sixtieth years of life. This is one of the great success stories of medicine. At the other extreme, psychology, for example, has not yet reached the stage of removing the major impediments to its own progress. The case against a psychological system of treatment such as psychoanalysis does not really rest on the fact that it is inefficacious—for that must be true of a great many forms of medical treatment—but on the fact that belief in psychoanalysis is an impediment to the discovery of the true causes of mental illness.

Dr. Comfort was doubtful about using replacement—transplantation methods, for example—as a cure or palliative for sterile deterioration, because ageing is essentially due to a multiple failure of homoeostasis. I think that is altogether too vague a description of ageing, because all human afflictions and infections in fact could be described as failures of homoeostasis. I don't think it will be possible to repudiate the idea of using replacement therapy until we have a theory of ageing, which we haven't got at present.

I would like to ask Dr. Koprowski his opinion of the relevance of our newer knowledge of polymorphism to the problem of resistance to infectious disease. It is a most important discovery that all large molecules—polypeptides, polysaccharides, and of course polynucleotides—exist in chemically and structurally variant forms in different individuals and these variant forms are not merely rare freaks maintained by mutation, but are present in the population in frequencies far higher than could possibly be maintained by mutation. According to genetical theory, which Haldane or Huxley may be able to uphold, all these variants are of medical significance, and if that is so, it must be one of the tasks of medicine to find out what that significance is. For example, the existence of these variants may make it virtually impossible for any one infective agent to overcome *every* member of the human population; there will always be a residue of individuals resistant to infection, no matter what the infective agent is. This indeed may be, as I think Haldane first suggested, the main reason for the existence of this genetical diversity.

Pincus: There is an ancient theory of ageing which should be mentioned, which dates back to certain ideas about rejuvenation. Essentially, it is dependent on the fact that a decline in secretory capacity of certain endocrine glands is accompanied by signs of infirmity. For some years we have been trying to find out about the situation in these glands. Among the steroid hormones, there is only one group, the 11-deoxy-17-ketosteroids, that tends to decline markedly with advancing age in the human species, both male and female. It is very interesting that these particular compounds appear to derive biogenetically from just one substance, 17-hydroxy-pregn-5-enolone. This is a key substance so far as hormones in ageing are concerned, because the rate of conversion of this substance to the 11-deoxy-17-ketosteroids declines with advancing age. We might try to find a method of keeping up this rate of conversion. I am inclined to think that this among others offers a chance for what Medawar calls replacement therapy—a replacement therapy of a very interesting nature.

Lipmann: In biochemistry we have sometimes found that with a very simple system one may get answers to a problem that ranges over a very wide field. Have we any definite information, for example, about the mechanisms of greying of hair? If we knew exactly why and how the colour of hair fails, we might know more about ageing. The activity of the enzyme dopa oxidase obviously must go down or become blocked.

Comfort: This loss of dopa oxidase certainly occurs at very different rates in different people. It also occurs in some follicles but not in others, for instance in genetic roaning in animals. White horses which lose their pigment start off fairly dark and whiten considerably as time goes on. It is not known exactly why it occurs, except that it is to some extent under genetic control.

Huxley: There is a particular breed of horse which gets whiter as it grows older and which tends to develop pigment tumours (melanomas) in a large proportion of cases.

Comfort: These are the greys, which have a different survival curve from any other horses.

Medawar: I think the greying of hair is actually due to loss of pigment-producing cells, melanocytes, from the hair bulb; once they have been lost they cannot be regenerated. One cause of loss could be radiation, and the greying of hair is in fact used as a measure of the incidence of ionizing particles on mice in outer space! Whatever the cause may be, it is cumulative and irreversible.

MacKay: Thinking about machines might help our understanding of one aspect of ageing. Suppose we had an artificial machine which was able to do intelligent "man-like" things. In principle such a machine could be everlasting, because repair men could plug in any part as soon as it needed replacement. The snag is that among other things we want it to store information; and a fault in an information store generally means an irreversible loss. Furthermore, a machine with a roughly-known life-span can be made vastly more effective for a given cost by embodying well-calculated compromises in the whole

principle on which it stores and retrieves information. One might, for example, get away with an analogue storage principle using traces which decayed slowly enough to match the average life-span.

We can see that with any such mechanism there would be a problem of senility quite apart from the problem of replacing its parts. I wonder whether—through the selective process, or whatever it is, by which our brains became the machines they are—the nervous system may not have committed itself to principles optimally matched to the life-span of the whole body. If so, then to multiply our life-span might land us with a different kind of problem.

Haldane: These last three papers have largely been a complaint against the fact that we are prisoners under sentence of death. I think that is slightly unreasonable, because although man is only able to move for very short distances, all the people in the world between them have lived for considerably longer than is commonly thought to be the age of the universe. Yet if they had all been to the Antipodes and all those journeys were put together, they would just about have got to *Alpha Centauri*, the nearest fixed star.

I am more worried by the prison than the sentence. Dr. Koprowski should come to India where we have any number of minor infections to deal with. Sulphaguanidine and emetine keep us on our feet if we survive the major diseases, which one can generally do now. Everybody here should read Act III, Scene 1 of *Measure for Measure*, in which the Duke of Vienna describes the molecular biology of his day:

> . . . Thou art not thyself;
> For thou exists on many a thousand grains
> That issue out of dust.

The speech is an admirable summary of what people thought was wrong with the human frame in Shakespeare's time.

Koprowski was perhaps, as he will probably be the first to admit, exaggerating a little. We have a new set of dangers in every generation, but seeing how well we have met many of

them in our own generation I think there may be enough intelligent people to deal with the emergence of resistant bacteria and the like. I am very glad that it is going to keep us on our toes, but we shan't be able to do it all by means of computers; we shall have to start thinking. Even if it means that a few million people will die prematurely every year, it is worth it in order to keep biologists on their toes, in my humble opinion.

If Dr. Szent-Györgyi would read the first act of Goethe's *Faust* he would find something rather similar to his idea about the mistake of pulling things apart. Goethe expressed it with much greater precision than I can. I am in entire agreement with Szent-Györgyi's point of view because I am a crass materialist; that is to say I think that it is probable that I am kept together by the same sort of agency as keeps a hydrogen atom or a larger molecule together. My only objection is to calling the things forces. I don't think they are anything like forces. The Indian *samkhyā* philosophy described them a good deal better, as what is called *sattra*, a principle of organization which is different from *rajas* (energy) or *tamas* (inertia). Until we start thinking in terms of quantal organization, rather than forces, I agree with Szent-Györgyi that we shan't get very far. I have a paper in the press with some ludicrous ideas about all that!

Lederberg: Some very interesting idealized abstractions have been brought up here which may play the same rôle in our theory of biology or bio-social dynamics that comparable abstractions do in physics, where, for example, the frictionless machine is an important concept in thinking about energy and entropy. We have heard of such abstractions as a germ-free world, indefinite life-span, and the intelligent self-reproducing machine. Each of these is quite possibly not attainable in its full form, but it doesn't need to be so in order to be well worth thinking about. These abstractions pose problems that we have to deal with either in emulating life or in setting up appropriate social dynamics in the clearest possible form. There is no point in arguing whether we will fully understand the system. We may never fully understand any mechanical

system, and yet it is of the utmost value to postulate one that is frictionless in order to isolate other elements of it.

The complete description of what would be wrong with a germ-free world, how to go about achieving it, how it could be maintained and what the imbalances are that might flow from it, might be much more intersting and provocative than any of the partial steps towards it, and perhaps we ought to discuss it in more detail. What fundamental basic limitations would there be in maintaining a germ-free world and what would be its danger? The implication is that it would be dangerous because we would be extremely vulnerable to the introduction of a single micro-organism which otherwise might not be pathogenic. Why is it pathogenic under those circumstances? Is it only necessary to maintain some reasonable level of activity of the reticuloendothelial system in order to have a ready response? In this case you could just take a shot of a mixed load of antigens every few weeks to keep yourself pepped up properly and you wouldn't have to worry too much about the next micro-organism. It is only by pushing these abstractions to the limit that we are going to be irritated into thinking about questions that are a little bit more general than the immediate ones of today.

Koprowski: Dr. Medawar answered his own question about polymorphism and resistance by stressing the rôle of the variant forms of large molecules in determining different responses of human subjects to exposure to an infective agent. The different permutations and combinations of genetic material which resulted in what Dr. Medawar calls chemical polymorphism of the human population have undoubtedly made it impossible for one pathogen to annihilate the human race. Although resistance of man to infections is conditioned by the genetic diversity of his molecular constituents, the actual *modus operandi* of these factors is unknown and should be thoroughly investigated in man himself. Studies of experimental animals were conducted. as I have pointed out in my talk, in genetically uniform breeds,

If the mechanism of resistance of man to a large variety of pathogens were to be unravelled, it might become possible to

imitate such resistance in a susceptible population by artificial means. We would still never be sure about the level of activity of human defence systems which would protect man against an attack by unknown pathogens, particularly of an extraterrestrial variety, but, following Dr. Lederberg's train of thought, the term "germ-free man" may become less of an abstraction. However, even then, if I had my way, I would implant man with a known concoction of living infective agents under controlled conditions rather than let him go germ-free into the world, which I cannot conceive will ever become "germ-free".

As far as the future of mankind is concerned, I may have painted a slightly darker picture than I originally intended and this may have accounted for Professor Haldane's comment. However, I have related my mild pessimism to the problem of human folly with its unlimited connotations.

Huxley: A germ-free world is an ecological absurdity, just as a perpetual motion machine is a mechanical absurdity.

Koprowski's comment about eradication is extraordinarily important. In most cases it is just nonsense to talk of eradication. We are coming up against that with these manufacturers of pesticides who say "Now we can eradicate such-and-such a pest". I am certain that it is not possible to eradicate any abundant pest, though it is quite easy to eradicate a non-abundant non-pest in trying to do so.

Talking of ecology, I was incidentally much interested in Koprowski's story about the bats spreading further north and west in America, and I wondered if this had anything to do with the secular improvement of climate in the past 50 years.

I am sure that one can get a lot of valuable ideas from considering problems like cancer and ageing on a comparative biological basis. For example, small birds and mice of comparable size have quite different patterns of life. They have very similar rates of development to maturity but the birds have a much greater total life-span. When mammals are treated with carcinogens there is a certain delay in the manifestation of the cancer. The delay is short in small mammals

like mice, much longer in man and larger mammals. If birds and mice of comparable size were treated with carcinogens would one find that the delay was correlated with the lifespan or with the rate of development to maturity?

There are some remarkable examples of purely genetic cancer caused by genetic imbalance, in fish like *Platypoecilus*, and plants like *Nicotiana*. In *Nicotiana* a number of species-crosses result in cancerous growths, which seem to be quite comparable to the cancerous growths in animals. One species, and certain individual chromosomes of the species, is especially effective in producing cancerous growths. There is a big opportunity for research here, since large quantities of plant cancerous tissue can be cultivated in organ-culture.

As Szent-Györgyi suggested, in studying any biological process one has to combine reductionist analysis with what I call *eduction*. This means first looking at the end-result of the process and its function, or its biological value. Then one can try to analyse it into its elementary components and origins, and finally see how the process works as a process—how it can be upset, how it can be improved.

There are some interesting sidelights on these problems. When I was at the Zoo, I got Dr. Honigmann to do some work on digestion in sloths and he found that this was almost as slow as their movements. What other basic phenomena of their life may be slowed down, I do not know. I don't even know if their expectation of life is very long.

I was once passing the enclosure of the giant Galapagos tortoises and I heard a very curious grunting noise, repeated regularly at considerable intervals. I eventually found it was made by the giant tortoises while they were copulating. If it had been speeded up ten times or so it would have sounded just like you or me!

Pirie: John Hunter, who is so thoroughly enshrined here at the Ciba Foundation*, also observed and measured the extreme slowness of digestion in the hibernating hedgehog.

* [The Ciba Foundation houses a small private museum of Hunteriana belonging to the Hunterian Society.]

Huxley: One would expect that, since its temperature is very low.

Pirie: But the delay is extremely long, up to a month or so, and it has always intrigued me that there was no rotting in the hibernating hedgehog. What is the antibiotic that keeps the hedgehog's gut fairly clean?

Medawar: I didn't understand quite what you meant, Dr. Szent-Györgyi, by talking about "complementarity" as a sort of vital property. What kind of property of the carbon atom is its valence? Is it a property of the carbon atom, or something rather vital and mysterious?

Szent-Györgyi: The mysterious thing to my mind, is that the biochemical system is much more complicated than we believed. One single molecule is an excessively complex entity which needs hundreds of numbers to specify its electronic distribution. To describe aromatics we used to draw hexagons and we thought we had then given a full description. Now we use hundreds of numbers in describing an exact fit of two molecules. If one molecule is changed, the other has to be changed, too, so that they still fit. The same holds true for the third molecule with which the second has to fit, and so forth. So, simultaneously, one has to change the whole system in a very precise manner. I cannot imagine this happening by random mutation. Changing one constituent only, we could make only trouble and not improvement.

Medawar: You declare that it is a mystery and then describe it lucidly!

Brain: You said that it is not explicable by natural selection.

Szent-Györgyi: Just random mutation would not do.

Hoagland: Why not? I disagree with that.

Szent-Györgyi: There are so many things which would have to happen simultaneously, in the most precise manner.

Hoagland: But natural selection is such a wasteful process in which every form of organization that survives represents thousands that have not. All we see are those that have survived. We have a tremendous screening process and it seems

to me that natural selection is an adequate way to account for these various survivals, even at the molecular level.

Huxley: Yes. Szent-Györgyi said he couldn't understand it happening by *mutation.* Of course nobody can understand it by mutation alone. Mutation is merely the raw material; it is natural selection that does the guiding and screening.

Szent-Györgyi: But one mutation wouldn't do; you must have many more simultaneously, or the whole system would no longer fit together. Then on top of all this, there is an additional complication: if the body has to build a substance, say protein X, it cannot do so directly. It must first have a factory which can turn out protein X; that is, it has to build the nucleic acid system into which it has to code the blueprint for protein X. All this becomes so complicated that I am unable to form a clear picture of how it all can happen. That is the mystery to me; maybe you understand it better.

Crick: I think you are a neo-vitalist, Dr. Szent-Györgyi, and it is characteristic of the neo-vitalist that he says he isn't! You made a great number of provocative statements, and apart from your remark on the hierarchies of organization, I think I disagree with almost everything you said, although I enjoyed your paper very much. Take, for example, the argument about the importance of quantum mechanics: I don't believe that a large new field relevant to chemistry remains to be discovered. Our basic knowledge of physics and chemistry is, I think, sufficiently complete for much of biology, though this is admittedly a very dangerous statement to make. Secondly, the argument about the amount of complexity is grossly exaggerated. The atomic nucleus is certainly extremely complex, and we do not in fact understand it, but the effect of changing the mass of the nucleus of an atom (a change which leaves its chemical properties intact) is extremely slight. Therefore, what one wants to know is, what are the *significant* alternatives involved, not just how complicated an atom is to put together. It also seems to me that mutation and natural selection are very powerful, and are potentially capable of explaining evolution.

Szent-Györgyi: I just want to wash my hands of vitalism: even if we don't need any new sciences, quantum mechanics will have to be greatly refined to be adequate for the analysis of most biological phenomena. At the moment, it is a very crude science which works with extremely inadequate methods. If I ask a physicist to calculate the jump of an electron from one level to another, he will need a few months, and a great number of computers, yet that electron makes the jump without computers and never misses. Maybe we need no new sciences and only have to perfect our present sciences very much. I would just remind you of the odd particles which physicists don't know what to do with. There is some very basic unknown law behind all this, so our knowledge must still be very incomplete.

Crick: The important thing you have to ask at each level is, do you understand it? It is perfectly true that we do not understand all quantum phenomena. What is interesting about molecular biology is that we can explain an enormous amount of it without knowing any quantum mechanics whatsoever. It is only for a few things like photosynthesis that you need to know quantum mechanics.

Szent-Györgyi: The function of a co-enzyme cannot be explained without quantum mechanics.

Crick: That is perfectly true when you get down to the chemical details, but from the point of view of vitalism we know that the same chemical reactions will go on in the test-tube in a very simple environment. It is not that there is anything mysterious or magical about it: it is simply that we don't understand chemistry to that degree of precision. But we can study the co-enzyme by chemical methods, and describe it by chemical methods, and then we can apply those to the biological context. You are asking that chemistry should be explained in terms of physics, whereas we are saying that one can explain biology in terms of physics and chemistry more easily than one would expect, although the step from physics to chemistry is rather difficult.

Szent-Györgyi: I disagree with that. You are mixing up two things. It is easy to reproduce a process, but that doesn't mean

we understand it. I produced muscle contraction in a bottle thirty-five years ago, and we still do not understand it.

Crick: That is because the system is genuinely complex. The basic reason why we don't understand muscular contraction is that the molecules involved are large, but we don't have to consider them right down to the atomic nuclei; we can describe them in terms of molecular structure, and the same applies to the genetic material. I agree with you that it is all very complicated, but not as complicated as you're trying to frighten us with.

Bronowski: I am on Crick's side in this argument. Now I want to stress the importance of these hierarchies of organization as levels also of our understanding of complex phenomena.

Let me explain this. I was interested in Szent-Györgyi's paper because I am in the process of trying to stop being a mathematician and trying to become a biologist. There are some things I find hard to understand, but there are some things I find it hard to understand why biologists don't understand. One of these is that quantum physics is not an isolated method, but is a by-product of a wider movement in our thinking. The new thought started with Darwin: it is that step-wise or other small forms of change become cumulatively fixed in new, stable organizations. This, as much as quantum physics, is part of statistical thinking.

Scientific explanation has moved through several stages in history. One stage was originated by Hobbes and Newton; theirs was the age when causal explanations suddenly clarified everything going on in the world. We are living in a time where statistical explanations are coming to have the same impact. But since we all grew up in a causal climate we still find it difficult to grasp the implications of the statistical outlook. In molecular biology, for instance, we have begun to understand the "geometrization" of organisms, but not yet its arithmetical implications. Szent-Györgyi is saying that when one tries to satisfy all the arithmetical demands of the geometry then one asks oneself: how on earth do the molecular units ever fit together? The answer is, they fit together by statistics.

They fit together because there are a great many of them, all seeking where they are going to fit; and when they find the fit, and only then, they are stable. This is an example of the transition from mechanistic to statistical thinking. Physicists have come to terms with this; they now know at what levels it is necessary to talk of individual quantum jumps, and at what levels it is good enough to consider only large integrations. But biologists are still struggling to learn this. Szent-Györgyi is still frightened by the detailed arithmetic which seems to be required. I remember being just as frightened in 1950 when I started some new work in electronics. How would I ever master the detail? And then I found that the young men who came to me could write wiring diagrams for electronic circuits as easily as other people write music. They knew how to think in units of the right level of organization. In the same way, biologists must now learn to think in the right statistical units.

Let me add a statistical footnote, Szent-Györgyi has calculated that altogether 10^5 people are going to die from existing doses of fall-out. That must be just about as many people as die in the world now in any 24 hours. I think that every individual life is precious; but I think we falsify our own values if we flourish 10^5 deaths as if they were a statistically large number.

Szent-Györgyi: The stability you have talked about may be the driving force I was aiming at, and I think about it a great deal. I should add that I would not condemn a hundred thousand people to death just because that many die anyway in a day.

MacKay: There is a missing element in our discussion which disturbs me. "Evolution" as an explanatory principle is rather like "money". We may (or may not) believe that "money can buy anything"; but if we want a new car we have also to ask whether the money we have is sufficient. There is a need to ask similar questions in any discussion of the adequacy of evolutionary explanation.

Thus in Szent-Györgyi's combinatorial problem, he stressed the complexity of the parameters that have to be "just right" for reproduction. But from the standpoint of information theory what one wants to ask is, how redundant is this complexity?

What statistical constraints are there between the parameters? How big is the selective job, and could it have been done in the time? This ought in principle to be an answerable question in terms of "amount of information". In other words, the discipline of information theory applies to the selective power of natural selection. Unless we argue in these terms, the issue is left to the man with the loudest voice.

Huxley: Muller made a big contribution to that in the *Scientific Monthly* in about 1930. He went a long way towards quantifying what changes could be achieved with a reasonable rate of mutation, and reasonable intensity of selection over the geological time-span available. The improbability of obtaining the observed results of evolution by chance mutation alone, without natural selection, is incredibly high.

Haldane: In a couple of papers which I called "The Cost of Natural Selection" I once tried to work out how many organisms would have either to die or to have their fertility reduced in order to get a single gene substitution. I came to the conclusion that if two mammalian species differ by something of the order of a thousand gene pairs, that agrees reasonably well with the time that the geologists think man has lived on earth.

MacKay: The difficulty is that each estimate depends on our present understanding of the complexity of the matching process involved. Each new discovery on the details of Szent-Györgyi's lock and key, if I may use that metaphor, may affect our calculations by an order of magnitude. The auditing of the evolutionary account seems to me to be an on-going process, not one that we can expect to close now. All we can say is that if things were as simple as in such-and-such a model, then there would be such-and-such a selective power in natural selection for a given time. But even this would be much better than baseless dogmatism.

Huxley: Surely it is a question of studying processes, and this is where I think that work like Waddington's is so illuminating. He points out that just as biological evolution by natural selection is essentially self-directed, so also is the epigenetic process of individual development. It is largely canalized into

adaptive channels by means of various homoeostatic processes.

Klein: As a biologist I feel a bit worried about non-biologists trying to tell us what biology is. Dr. Bronowski said that biological thinking started with Darwin. I am full of respect and admiration for Darwin, but the word biology emerged much earlier, in 1802. It came from three quite different places: from Lamarck in France, and from Treviranus and Burdach in Germany. This word, which had not existed earlier, appeared in the period of romanticism. This kind of romantic thinking is not quite forgotten today and has at least some echoes in biology and medicine. I am quite aware that 1859 was a date of enormous importance in human thinking, but it was not the starting point of biological thinking.

Bronowski: You are right, except that I would also quote Darwin's grandfather, Erasmus Darwin, who lived before 1802. However, it was not biological thinking, it was statistical thinking that was derived from Darwin. The leading physicist who started statistical mechanics, Ludwig Boltzmann, acknowledged that the theory of natural selection had influenced him to view the behaviour of gases statistically.

Klein: But to go back to the historical point of view, Darwin said several times that his theory came through Malthus, and Malthus published his views first in 1798.

Huxley: Darwin's theory didn't come from Malthus, although he was stimulated to think of his theory by reading Malthus. Malthus stressed the pressure of population on resources, but had no idea of selection.

Klein: Dr. Szent-Györgyi, why do you feel you must wash your hands of vitalism? Vitalism is not a shame or a sin. The old vitalism of Stahl is dead, but I think that all medical men here would agree that we can't think without—I shouldn't say vitalism—but something different from a physicochemical explanation. MacKay has talked about the action of force on force and the action of form on form, and I had the feeling that between force-force and form-form was the gap between the physical explanation and the biological explanation. I agree that with biology we are in a new world.

Medawar: If vitalism is such a valuable method of thinking, would you give us a valuable thought?

Klein: I don't say that vitalism is a valuable way of thinking, but I am quite sure that in all that we are doing in human biology, we cannot work with physical and chemical models alone.

MacKay: In saying this, surely you are saying something which would also be true of engineering? The change from discussing the action of force on force to discussing the action of form on form is characteristic of any change from a pure to an applied science. It characterizes our way of talking about both living and non-living teleological (cybernetic) mechanisms.

Klein: Teleology is akin to vitalism.

MacKay: But cybernetics typically reinstates teleological forms of thought without denying the adequacy of physical explanation at its own level. This is why so many of us don't like the term vitalism. Vitalism is not a positive term for most people but a negative one; it stands for a "postulate of impotence" at the physical level. There is no postulate of impotence involved in accepting the cybernetic way of describing a living system. It implies, not that explanation at the physical level is impossible, but merely that it misses the point revealed in teleological terms.

Klein: The man who fought vitalism hardest was Claude Bernard, and once he had finished fighting vitalism he brought in the *idée directrice* and the *milieu intérieur.*

Huxley: MacKay used the word teleological. I would prefer him to use the word *teleonomic* which was introduced into biology a few years ago. This does not imply, as the term teleological usually does, that there must be a conscious purpose behind evolution, but that it is automatically, or if you like, homoeostatically, directed to some functional end.

Comfort: Perhaps the model that Dr. MacKay was looking for was the thing which was worrying Dr. Szent-Györgyi about the coincidence of successive mutations. I believe some work has been done on the analogy of the anagram where you start

with a word and you have to change it to another word of the same number of letters without writing down any word which makes nonsense. It is a question of a model which would give you successive mutations which must be biologically significant.

Huxley: Lewis Carroll invented that game; he called it Doublets.

Bronowski: You are talking about making an anagram, a sensible word, from a set of letters. The thing that we are all saying about levels of organization comes to this: natural systems work by making anagrams—arranging letters into individual syllables, say; then by finding words which can be made out of the syllables; and then by making sentences out of the words. Once you have thought of that analogy, it is a great illumination.

Genetic Progress by Voluntarily Conducted Germinal Choice *

HERMANN J. MULLER.

IT HAS become a cliché in some circles that natural selection cannot be hindered, no matter what we do, because the organisms that survive and multiply are of course, *ipso facto*, the fittest[1]. The implication of this seems to be that we might as well have a good time in any way we like, and that there is nothing to be feared, or helped either, at least genetically, in this best of all possible worlds.

This pseudo-philosophical literalism ignores the evidence that the great majority of species have perished without issue. Most often this has been because the natural selection in their line was outsmarted, or rendered outmoded, by developments elsewhere. In other cases it has been because the natural selection led to the adoption of traits that favoured the possessors of them and their immediate descendants, as compared with other individuals of the same population, but worked to the disadvantage of the population as a whole, over the long term. True, the division of a species into many small groups or sub-groups, that eventually competed with one another, tended to check such miscarriages of natural selection to some extent, and could even exert an overriding influence in the opposite direction. However, the type of balance or of flux attained between these conflicting forces depended on the specific situation that existed. Hence, no generalization could be valid that declared all species to be foreordained to rise by natural selection.

There were similar flaws in the naive egalitarianism according to which all species must be equally fit, at least for their

* This paper was read by Dr. Wolstenholme because Professor Muller was unfortunately prevented by illness from participating in the symposium.

own niches, in consequence of all of them alike having been products of a natural selection that got them here contemporaneously. This doctrine resembles in principle the cultural egalitarianism that some anthropologists apply to all coexisting human societies. In both cases two major points have been disregarded. These are that evolution proceeds, under different circumstances and for different groups, at very different speeds, and—more important—that it varies greatly in the degree to which it is *progressive*. As Julian Huxley has often emphasized[2,3], the concepts of "progress", and of "higher" and "lower", as applied to biological evolution, correspond with objective realities.

The higher forms, those resulting from the more progressive evolution, have elaborations that allow them to overcome more and greater natural difficulties, and even to turn more refractory circumstances to their actual advantage. True, their weight of extra accoutrements tends to keep them from carrying out the *easiest* tasks so readily, and niches are thereby left in which the more primitive or lower forms can continue to thrive also. Nevertheless, the higher forms, by virtue of their more advanced capabilities, are on the whole more likely than the others to succeed in adapting to even more difficult situations in the future. That is, they tend, at least in their heyday, to have superior evolutionary potentialities, and thus to constitute stem forms for further advances. This is another illustration of the principle: "to him that hath shall be given". Yet even among higher organisms it is a rare species that succeeds in putting forth new shoots that persist long and develop much further; it is far more likely to enter an evolutionary *cul-de-sac*, as the fossil record attests.

THE DIRECTION TAKEN HITHERTO BY NATURAL SELECTION IN MAN

In the line of ancestry that led to man, and in his further biological ascent, the already existing genetic constitution conferred unusual faculties of manipulation, co-operation, communication and general intelligence, along with a posture that facilitated their use, and these faculties, working in conjunction,

must have constituted critical factors that favoured man's survival. It is obvious, therefore, that under primitive conditions of living those faculties in our pre-human and early human ancestors must have become enhanced by natural selection. These same faculties, moreover, after having become sufficiently enhanced in their genetic basis, made possible an increasing mental transfer from individual to individual and from generation to generation of the lessons and skills acquired by experience, and thus gave rise to the process of extra-genic accumulation of learned reactions that we call cultural evolution.

For a long time there must have been a considerable positive feedback from cultural to genetic evolution[4c]. Some of the comparatively advanced and demanding practices instituted by culture must inevitably have called forth keener forms of competition between individuals, and between small groups of them. These practices would include more sophisticated types of communication and of mutual aid, which would better serve the interests of the given family or small community, in its direct or indirect competition with other groups. Thus culture itself provided a basis for more effective natural selection in favour of the very traits that advanced that culture.

For a further understanding of the influence of culture upon biological constitution, it is important to recognize certain other principles concerned with the operation of natural selection. It is easy to see that greater ability of any kind, physical or mental, exerted on behalf of its possessor, has a selective advantage and tends in the course of generations to become established in a population. It is also evident that predispositions to be of service to others of the immediate family will be of selective advantage, because the operations of these predispositions will promote the survival and multiplication of replicas of the very genes that gave rise to them. In other words these actions, although altruistically directed, are in essense *reflexive* in that they foster, through their selective influence on others, the multiplication of the same type of genes as they themselves derive from. This is in a sense an extension of genetic selfishness or, if you prefer, an enlightened, limited altruism.

A similar situation exists, but the selective pressure is weaker, in cases of genes that lead the individual to help not just his immediate family but also others of a small, genetically closely related group to which he belongs. For in directing his help preferentially to them he is, again reflexively, tending to help the multiplication of whatever distinctive genes had been operative in this behaviour, since these genes are likely to exist in greater concentration among his relatives than among other individuals taken at random. Obviously, however, the larger the community to which he extends such help, the lower is the relevant resemblance between his genetic constitution and theirs, and the weaker, for that reason, is the resulting reflexive selection. Moreover, when groups are larger they are fewer, and then offer correspondingly less choice for any process of selection which, like that under consideration here, operates among them as wholes. Thus, selection for altruistic propensities has tended to work chiefly for those traits that cause help to be given very near to home[5].

An additional factor lies in the survival value of such feelings of reciprocity as are represented by the expression "I help him who helps me". For these feelings may arise between unrelated individuals and even in such a case they are by their nature reflexive. That is, they tend to redound to the benefit of the first participant, and so to the multiplication of the very genes that underlie the given social feelings. It should be noted, however, that this process does not include selection for the impulse to turn the other cheek or to love one's enemy: quite the contrary, for a form of reciprocative disposition would tend to be selected which, though returning help for help, also gave blow for blow, or took an eye for an eye, since that behaviour also is reflexive, by affording defence to one's own genes.

However, cultural progress inevitably led men into ever larger associations, which tended to engulf or squeeze out the smaller groups. Thus even strangers had to learn to behave amicably towards one another, and according to generally accepted rules of conduct. Under these circumstances the principle of reciprocation, applied to strangers, both privately and publicly, must

have resulted in some selection in the direction of making such behaviour tolerable and not entirely hypocritical. At the same time, even in the great civilizations of ancient and mediaeval times charity began at home and there must have remained a severe struggle for existence in which those genetic lines prospered more whose genes were so constituted as more effectively to serve "number one", and "number one junior", and the others in the little family conspiracy.

It might at first sight be surmised that natural selection was inevitably reduced under the circumstances of civilization. However, in both barbaric and civilized societies of the past the size of the population tended to rise in step with its increase in productive capacity. It followed that the ordinary individual and his family remained about as close as ever to the economic level where their survival was in jeopardy. Under these circumstances, whether or not they tended to die out or to multiply, relatively to the rest, depended for the most part on the efforts of that same person or family (despite some notable exceptions to this rule, as in the Inca empire and among Pueblos). Consequently, natural selection must have continued within civilized populations to enhance whatever social traits led people primarily and actively to serve their own family, and, secondarily, to get along with their other associates to a degree sufficient for eliciting the latters' good will. At the same time, however, as previously explained, there could no longer be as high a genetic premium on service to the whole community as when the communities were smaller, more numerous, and subject to more genetic isolation from one another.

THE NEGATIVE FEEDBACK ESTABLISHED BY MODERN CULTURE

Modern technologies and social organization, working in combination, have altered the manner of operation of selection much more drastically than this in those typical industrial societies in which the increase in the means of subsistence has been greater than the increase in the size of population. Not only is there in these societies an ever more rapid disappearance of that genetic isolation between small groups which underlies

natural selection for truly social propensities; there is also a disappearance of the circumstances that have favoured the survival and multiplication of individuals genetically better fitted to cope with difficulties and that, conversely, have led to the dying out of lines deficient in these faculties. For society now comes effectively to the aid of those who for whatever reason, environmental or genetic, are physically, mentally, or morally weaker than the average. True, this aid does not at present afford these people a really good life, but it does usually succeed in saving them and their children up to and beyond the age of reproduction.

It is probable that some 20 per cent, if not more, of a human population has received a genetic impairment that arose by mutation in the immediately preceding generation, in addition to the far larger number of impairments inherited from earlier generations. If this is true, then, to avoid genetic deterioration, about 20 per cent of the population who are more heavily laden with genetic defects than the average must in each generation fail to live until maturity or, if they do live, must fail to reproduce. Otherwise, the load of genetic defects carried by that population would inevitably rise. Moreover, besides deaths occasioned by circumstances in which mutant genes play a critical rôle, there is always a large contingent of deaths resulting from environmental circumstances. Consequently, the number of individuals who fail to "carry along" must considerably exceed 20 per cent, if genetic equilibrium is to be maintained, and *merely* maintained. Yet among us today, in industrialized countries, the proportion of those born who fail to reach maturity has fallen to a small percentage, thanks to our present high standards of medicine and of living in general. This situation would, other things being equal, spell genetic deterioration, at a roughly calculable rate.

However, it has sometimes been surmised that the present excess of genetically defective adults—those whose lives have been saved by modern techniques—may somehow be screened out, after maturity, through the automatic operation of an increased amount of reproductive selection, in that these

additional defectives (or an equivalent excess of others) fail to have offspring. However, it would be wishful thinking to suppose this to be the case. There is no evidence of an over-all positive correlation today between effective reproductive rate and soundness of body, mind, or temperament, aside from cases of extreme defect too rare to influence the trend to an important extent.

On the contrary, negative partial correlations have repeatedly been found between reproductive rate, on the one hand, and the rank of the parents in such social classifications as economic status or education, on the other hand. This has been the case not only in the Western world but even in the U.S.S.R. Now educational and economic status, although certainly not genetic categories, do have important genetic contingents, especially in societies not having very rigorous class divisions. Moreover, it is hardly credible that the factors that give rise to the observed negative correlations would be able to distinguish between the differences that depend on environmental influences and those that depend on genes, so as to allow the environmental differences but not the genetic ones to be responsible for all of the negative correlations found. We therefore return to the conclusion that genetically based ability and reproductive rate are today negatively correlated.

Attacking the matter from another angle, a consideration of the attitudes and practices of people in general, in technologically advanced societies, provides telling clues concerning the most prevalent causes of present-day differences in family size. It is obvious that in the main these differences no longer depend, as they did in the past, on how many children the person or couple are able to have, but rather on, first, the extent to which they aim to limit conception and, second, the extent to which they succeed in attaining this aim. It is not the having of children but the prevention of them which today requires the more active, responsible effort, an effort which makes demands on the participants' prudence, initiative, skill, and conscience.

It seems evident that persons possessed of greater foresight, and those with keener regard for their family, usually aim to

have a lower than average number of children, in order that they may obtain higher benefits for those children that they do have, as well as for themselves and others near to them. Moreover, persons who experience failure in their work, their home life, or their health, are especially likely to seek compensatory gratification in having children. At the same time, as regards success in limiting conception to the extent aimed at, it is evident that ability enters in here in a negative way, in that those who are clumsier, slacker, less provident, and less thoughtful are the very ones most likely to fail in keeping the number of their children down to whatever quota they may have set. It is possible, therefore, that selection based on differences in reproductive rate is today not merely inadequate to maintain genetic fitness against the pressure of mutation (using the word fitness here in its larger sense, that of having a constitution valuable for the population as a whole), but that such selection is today working actively in reverse, so as to decrease fitness.

THE HUMAN GENETIC PREDICAMENT

This is an ironical situation. Cultural evolution has at long last given rise to science and its technologies. It has thereby endowed itself with powers that—according to the manner in which they are used—could either wreck the human enterprise or carry it upward to unprecedented heights of being and of doing. To steer his course under these circumstances man will need his greatest collective wisdom, humanity, will to co-operate, and self-control. Moreover, he cannot muster these faculties in sufficient measure collectively unless he also possesses them in considerable measure individually. Yet in this very epoch cultural evolution has undermined the process of genetic selection in man, a process whose active continuance is necessary for the mere maintenance of man's faculties at their present none-too-adequate level. What we need instead, at this juncture, is a means of *enhancing* genetic selection.

True, there are specialists who believe that equivalent or even better results than selection could provide may be obtained by

direct mutagenic operations on the genetic material. In addition, some of them think that much could be done by modifying development and physiology, and by supplying much more sophisticated, more or less built-in, artificial aids. Others, disgusted with the limitations and the patchwork constitution of all natural organisms, boldly say that completely artificial contrivances can and should be built to replace mankind[6].

Let all these enthusiasts try their tricks, the more the merrier. But I find myself a conservative on this issue. It seems to me that for a long time yet to come (in terms of the temporal scale of human history thus far), man at his present best is unlikely to be excelled, according to any of man's own accepted value systems, by pure artifacts. And although artificial aids should become ever better developed, and integrated as harmoniously as possible with the human organism, it is more economical in the end to have developmental and physiological improvements of the organism placed on a genetic basis, where practicable, than to have to institute them in every generation anew by elaborate treatments of the soma.

Finally, as regards changes in the genetic constitution (genotype) itself, there is certainly enormous room for improvement. However, the genetic material of man is so transcendently complex in its make-up and workings that for some centuries, at least, we should be able to make genetic progress on a wider front, with better balance, and more rapidly, by selecting among the genotypes already on hand, whose physical (phenotypic) expressions have been observed, than by intervening with what I call nano-needles* to cause pre-specified changes in them. At any rate, we will be much more likely some day to attain such finesse if we are forthright enough to make use, in the meantime, of the cruder methods that are available at present.

Man as a whole must rise to become worthy of his own best achievements. Unless the average man can understand and appreciate the world that scientists have discovered, unless he can learn to comprehend the techniques he now uses, and their remote and larger effects, unless he can enter into the thrill of

* Nano-needles = micro-micro needles.

being a conscious participant in the great human enterprise and find genuine fulfilment in playing a constructive part in it, he will fall into the position of an ever less important cog in a vast machine. In this situation, his own powers of determining his fate and his very will to do so will dwindle, and the minority who rule over him will eventually find ways of doing without him. Democratic control, therefore, implies an upgrading of the people in general in both their intellectual and social faculties, together with a maintenance or, preferably, an improvement in their bodily condition.

PROPOSED WAYS OUT OF THE PREDICAMENT

Most eugenists of the old school believed they could educate the population so as to lead the better endowed to have larger than average families and the more poorly endowed to have smaller ones. However, people are notoriously unrealistic in assessing themselves and their spouses. Moreover, the determination of the size of a family is, as we have seen, subject to strong influences that tend to run counter to the desiderata of eugenics. In view of this social naïveté on the part of the eugenists in general, as well as the offensively reactionary attitude flaunted by that vociferous group of eugenists who were actuated by race and class prejudices, it is not surprising that some three-quarters of a century of old-style eugenics propaganda has resulted in so little actual practice of eugenic principles by people in general.

It is true that heredity clinics have recently made some headway and are in themselves highly commendable. However, the matter of choice of marriage partners, with which they concern themselves so much, has little relation to the eugenically crucial matter of gene frequencies. And so far as their advice concerning size of family is concerned, it is for the most part confined to considerations arising from the presence of a gene for some rare abnormality. For any individual case such a matter is of grave importance. Yet for the eugenic pattern as a whole the sum of all such cases is insignificant in relation to the major task of achieving a high correlation between the over-all genetic

endowment and the rate of reproduction. However, counsellors would understandably hesitate to be so cavalier as to assign people over-all ratings of so comprehensive a nature, and if they did so their advice would probably be resented and rejected.

Similarly, the public in a democratic society would probably be unwilling to adopt social or economic rearrangements that were known to have as their purpose the encouragement of large families on the part of certain occupational groups, whose members were considered eugenically more desirable, and the making of reproduction less attractive for other occupational groups, considered genetically inferior. Moreover, the public's objections to the introduction of such programmes would probably remain even if the people concerned were allowed the deciding voice in their choice of occupation.

Perhaps such considerations as these have played a part in leading Dr. P. B. Medawar[7] and some others to conclude that consciously directed genetic change in man could only be carried out under a dictatorship, as was attempted by Hitler. As they realize, a dictatorship, though it might hoodwink, cajole and compel its subjects into participation in its programme, would try to create a servile population uncomplainingly conforming to their rulers' whims. That would constitute an evolutionary emergency much more immediate and ominous than any gradual degeneration occasioned by a negative cultural feedback.

If all these proposed means of escaping our genetic predicament are impracticable, insufficiently effective, or even positively vicious, what other recourse is available for us? To consider this problem we must rid ourselves of preconceptions based on our traditional behaviour in matters of parentage, and open our minds to the new possibilities afforded by our scientific knowledge and techniques. We shall then see that our progress along certain biological lines has won for us the means of overcoming the negative feedback with which we are here concerned. We can do so by bringing our influence to bear not on the number of children in a family but on their genetic composition.

The method that first brought this possibility into view is of course that of artificial insemination with semen derived from a donor, "AID". Unlike what occurs in the usual practice of AID, however, the germinal material here is to be chosen and applied primarily with a view to its eugenic potentialities. Preferably it should be selected from among banks of germ cells that have been subjected to long-term preservation (see, for example, references 2, 4b, 4c, 5, 8, 9).

It was long ago found that human semen will recover from freezing, even from deep-freezing, and that in the latter state it can probably be preserved indefinitely. Glycerol and other additives have been found by Drs. Polge, Parkes, Sherman and others to aid the process. Such preservation will allow the accumulation of larger, more diverse stores, their better appraisal, and the fading away of some of the personal biases and entanglements that might be associated with the donors. At first sight the most unrealistic of the proposals made, this method of *eutelegenesis* or *germinal choice*, turns out on closer inspection to be the most practical, effective, and satisfying means of genetic therapy. This is especially true, the more reliable and foolproof the means of preventing conception are.

THE ADVANTAGES OF GERMINAL CHOICE

The Western world is a chrysalis that still carries, over its anterior portion at least, a Victorian-looking shell, but wings can be discerned lying latent beneath the surface. Despite the protests of some representatives of traditional ways and doctrines, a little searching shows that a considerable section of the educated public, including outstanding leaders in law, religion, medicine, science and education, is prepared to take a sympathetic interest in the possibilities of germinal choice. As for the public at large, that of the United States, which has on the whole been more bound than that of Europe to old-fashioned ways, is now taking in its stride the practice of AID for the purpose of circumventing a husband's sterility. In fact, it is estimated[10] that five to ten thousand American children per year are now being engendered in this way, and the number is

growing rapidly. In addition, an increasing number of couples are applying for AID in cases where the husband carries or has a strong chance of carrying some grave genetic defect, or some constitutional trait (of an antigenic nature, for instance) that may be incompatible with a trait of his wife's. Moreover, a few of the practitioners of AID are already making it a point to utilize, where feasible, germinal material from donors of outstanding ability and vigour, persons whose genuine merits have been indicated in the trials of life. Studies of the family life in AID cases have shown it to be, in general, unusually well adjusted.

When to these developments we add the fact that several banks of frozen human semen are even now in operation, in widely separated localities, we see that a thin line of stepping stones, extending most of the way to germinal choice itself, has already been laid down. It is but a short step in motivation from the couple who wish to turn their genetic defect to their credit by having, instead, an especially promising child, to the couple who, even though they are by no means subnormal, are idealistic enough to *prefer* to give their child as favourable a genetic prospect as can be obtained for it. There are already persons who would gladly utilize such opportunities for their families. These are persons who, as my friend Calvin Kline has put the matter, take more pride in what they can purposively create with their brains and hands than in what they more or less reflexly produce with their loins, and who regard their contribution to the good of their children and of humanity in general as more important than the multiplication of their own particular genetic idiosyncracies. Once these pioneers have been given the opportunity to realize their aspirations, and to do so without subterfuge, their living creations of the next generation will constitute a sufficient demonstration of the worth of the procedure, both for the children themselves, for their parents, and for the community at large.

There are, however, several requirements still to be met before germinal choice can be undertaken on even a pilot scale. A choice is not a real one unless it is a multiple choice, one carried

out with maximum foreknowledge of the possibilities entailed, and hampered as little as possible by irrational restrictions and by direct personal involvements. Moreover, to keep as far away as possible from dictation, the final decision regarding the selection to be made should be the prerogative of the couple concerned. These conditions can be well fulfilled only after plentiful banks of germinal material have been established, representing those who have proved to be most outstanding in regard to valuable characteristics of mind, heart, and body. In addition, such storage for a person's own germ cells should be a service supplied at cost to anyone wishing it. Catalogued records should be maintained, giving the results of diverse physical and mental tests and observations of all the donors, together with relevant facts about their lives, and about their relatives.

The couple making a choice should have access to these records and the benefit of advice from physicians, psychologists, geneticists, and specialists in the fields in which the donors had engaged. The germinal material used should preferably have been preserved for at least twenty years. Such an undertaking by a couple would assume the character of an eminently moral act, a social service that was in itself rewarding, and the couple who engaged in it would be proud of it and would not wish to conceal it.

We have not here touched upon any of the more technical genetic matters that would ultimately be involved in human betterment, because at this stage the important task is to achieve the change in *mores* that will make possible the first empirical steps. When the choices are not imposed but voluntary and democratic, the sound values common to humanity nearly everywhere[4b] are bound to exert the predominant influence in guiding the directions of choice. Practically all peoples venerate creativity, wisdom, brotherliness, loving-kindness, perceptivity, expressivity, joy of life, fortitude, vigour, longevity. If presented with the opportunity to have their children approach nearer to such goals than they could do themselves, they will not turn down this golden chance, and the next generation, thus

benefited, will be able to choose better than they did. The broadness of the base constituted by the population of choosers themselves will ensure that they also perpetuate a multitude of special faculties of mind and body, which they severally regard especially highly. This will promote a salutary diversity.

Undoubtedly further techniques are in the offing that will radically extend the possibilities of germinal choice. Among these are, perhaps, the storage of eggs. Still more important is the working out of methods for obtaining normal development of germ cells outside the body, using immature germ cells a supply of which can be stored in deep-freeze, to be tapped and multiplied at will. Clonal reproduction, as by the transfer of unreduced nuclei to eggs, would be another milestone[11]. Beyond all that are of course more delicate methods of manipulating the genetic material itself—what I have termed the use of nano-needles. Yet long before that we must do what we can. One could begin by laying up plentiful stores of germ cells for the future. Their mere existence will finally result in an irresistible incentive to use them. Man is already so marvellous that he deserves all our efforts to improve him further.

SUMMARY

Modern civilization has instituted a negative feedback from cultural progress to genetic progress. This works by preventing the genetic isolation of small groups, by saving increasing numbers of the genetically defective, and by leading the better endowed to engage more sedulously than others in reproductive restraint. Yet the increasing complications, dangers, and opportunities of civilization call for democratic control, based on higher, more widespread intelligence and co-operative propensities.

The social devices and the individual persuasion regarding family size advocated by old-style eugenics are inadequate to meet this situation, except in extreme cases of specific defects. For the major problem, concerned with quantitative characters, the more effective method and that ultimately more acceptable psychologically is germinal choice (Brewer's *eutelegenesis*).

Artificial insemination, now used for circumventing sterility, can, by becoming more eugenically oriented, lay a foundation for this reform. For this purpose it must become increasingly applied in cases of genetic defect, genetic incompatibility, suspected mutagenesis, postponed reproduction, and finally, in serving the ardent aspiration to confer on one's children a highly superior genetic endowment.

For realizing these possibilities extensive germ-cell banks must be instituted, including material from outstanding sources, with full documentation regarding the donors and their relatives. Both lengthy storage and donor distinction will promote the necessary openness and voluntariness of choice, and aid the counselling. The idealistic vanguard, and those following them, will foster sound genetic progress by their general agreement on the overriding values of health, intelligence, and brotherliness. Their different attitudes regarding specialized proclivities will foster salutary diversities.

Biological Future of Man

JOSHUA LEDERBERG

DARWIN's theory set off the historic debate on man's past. Today, with a new biology we mirror his future. Poetry may speak more bravely than Science. However, Policy must rely on Science for an accurate vision of the bounds of human evolution.

MOLECULAR BIOLOGY

Molecular biology has lately unravelled the mechanism of heredity, and we can say that the main features of terrestrial life are within the perceptible grasp of experimental chemistry. Many of its puzzles have already worked out with astonishing simplicity. The basic strategy of life is that of molecular structure. The linear, bi-helical structure of deoxyribonucleic acid (DNA) (and who would have thought that genes would be resolved before tendons?) tells us the mechanism of molecular reproduction—the selection of nuclein molecules that have a complementary fit to the available space on the existing DNA chain. We have also a fair picture of how the nuclein sequence in DNA is translated into the corresponding sequence of amino acids in proteins. And the coiling of the amino acid chain, determined by this sequence, generates the three-dimensional shape by which the protein works. The protein molecules, by a similar fit of shape, recognize one another to aggregate into structural fibres and membranes, or enfold smaller molecules to direct the metabolic flow chart of the cell.

Now we can define man. Genotypically at least, he is six feet of a particular molecular sequence of carbon, hydrogen, oxygen, nitrogen and phosphorus atoms—the length of DNA tightly coiled in the nucleus of his provenient egg and in the nucleus of

every adult cell, 5 thousand million paired nucleotide units long. This store of "information" could specify 10 million kinds of proteins. Almost certainly, most of this information controls just when and where some few thousands of proteins will be made—the tendons and enzymes, antibodies, hormones and the like, of which the body is composed.

Evolution is the duplication and exploitation of structural error. Simple organisms have as few as 100,000 units (the even simpler viruses plagiarize the larger genetic "library" of their host cells). Mistakes in molecular reproduction—mutations—are inevitable: one of evolution's marvels is that they are so rare. The innovation rarely serves better; when it does, the cell that carries the mutant DNA will be favourably selected, and the new DNA thus preferentially propagated in future generations.

From principle to detail is still a big step. We do not in fact yet know the actual nucleotide sequence of any gene. Only in micro-organisms, whose DNA content is from a millionth to a thousandth of man's, can we momentarily substitute one DNA molecule for another in the genetic composition of a cell, and then inferentially judge the chemical differences between them. But a little inspiration and reasonable effort will be rewarded by detailed knowledge of genetic structure, very soon for microbes, no more than a decade or so away for parts of the human genome.

EUGENICS AND EUPHENICS

Most geneticists, however they may be divided on their specifications for policy, are deeply concerned over the status and prospects of the human genotype.

Human talents are widely disparate; much of the disparity (no one suggests all) has a genetic basis. The facts of human reproduction are all gloomy—the stratification of fecundity by economic status, the new environmental insults to our genes, the sheltering by humanitarian medicine of once-lethal defects. Even if these evils were tolerable or neutralized or mis-stated, do we not still sinfully waste a treasure of knowledge by ignoring the creative possibilities of genetic improvement? Surely the

same culture that has uniquely acquired the power of global annihilation must generate the largest quota of intellectual and social insight to secure its own survival?

The recent achievements of molecular biology strengthen our eugenic means to achieve this purpose. But do they necessarily support proposals to transfer animal husbandry to man? My own first conclusion is that the technology of human genetics is pitifully clumsy, even by the standards of practical agriculture. Surely within a few generations we can expect to learn tricks of immeasurable advantage. Why bother now with somatic selection, so slow in its impact? Investing a fraction of the effort, we should soon learn how to manipulate chromosome ploidy, homozygosis, gametic selection, full diagnosis of heterozygotes, to accomplish in one or two generations of eugenic practice what would now take ten or one hundred. What a clumsy job we would have done on mongolism even just five years ago, before we understood the chromosomal basis of this disease! No one would undertake a costly programme of animal improvement without a clear cut engineering design from which we could compute the anticipated benefits in relation to the costs.

As further extensions of experimental cytology, we might anticipate the *in vitro* culture of germ cells and such manipulations as the interchange of chromosomes and segments. The ultimate application of molecular biology would be the direct control of nucleotide sequences in human chromosomes, coupled with recognition, selection and integration of the desired genes, of which the existing population furnishes a considerable variety.

These notions of a future eugenics are, I think, the popular view of the distant rôle of molecular biology in human evolution, but I believe that they mis-state its real impact on human biology in the near furure. What we have overlooked is *euphenics*, the engineering of human development.

Development is the translation of the genetic instructions of the egg, embodied in its DNA, which direct the unfolding of its substance to form the living, breathing organism. The crucial problem of embryology is the regulation and execution of

protein synthesis which underlies the orderly differentiation of cell types—how some DNA segments are made to call out their instructions and others are suppressed. These issues are now suddenly accessible to experimental analysis. Embryology is very much in the situation of atomic physics in 1900; having had an honourable and successful tradition it is about to begin! But it will not take long to mature. Most predictions of research progress have proved recently to be far too conservative.

Until now, the major problems of human development—not only embryology, but also the phenomena of learning (in its neurobiological aspects), immunity (with its bearing on transplantation), neoplasia and senescence—could be approached at only the most superficial level. They are about to be transformed in the sense that genetics has been, as epiphenomena of protein and nucleic acid synthesis. The present intensity of effort suggests a span of from five to no more than twenty years for an analogous systematization. The application of these advances to human affairs is equally imminent.

On these premises it would be incredible if we did not soon have the basis of developmental engineering technique to regulate, for example, the size of the human brain by prenatal or early postnatal intervention. In fact, it is astonishing how little experimental work has been done to test some elementary questions on the hormonal regulation of brain size in laboratory animals or the functional interconnexion of supernumerary brains. Needless to say, "brain size" and "intelligence" should be read as euphemisms for whatever each of us projects as the ideal of human personality.

The basic concept of molecular biology is the chain of information from DNA to ribonucleic acid (RNA) to protein. We are just beginning to ask questions about mental mechanisms from this standpoint. The simplest and one of the oldest suggestions about memory is the modification of neuronal interconnexion through control of synthesis and deposition of durable proteins at the interfaces. The link between electrical impulses and protein synthesis could easily be the accompanying shifts of potassium and sodium ion concentrations, these ions being

also important cofactors for several enzymes involved in protein synthesis. More elaborate coding, such as the modulations of the actual conformation of the proteins can also be invoked, but may not be necessary to account for the actual storage capacity of the brain. Speculative models for this kind of coding can be built on the basis of present knowledge of protein synthesis, without impairing the conservation of information in the nucleic acids or invoking unsubstantiated principles of electrical control of nucleic sequences. Unlike other cellular systems, the neurones, which rarely if ever divide, need no mechanism to propagate their information to cell progeny. The burden of data storage may therefore be confided entirely to protein.

The purpose of mentioning these speculations is to dramatize the relationship of mental science to molecular biology. The analysis of protein structure and metabolism throughout the brain, the correlation of structural development with learning, its genotypic control, and its alteration in disease are beginning to be attacked in force, impelled in part by social concern for the immensely important problem of mental retardation, as such research must tell us even more about normal mental development.

In another field of developmental engineering Professor Medawar has already exhibited a *tour de force*, the abolition of immunity to transplants introduced in early life, a work which has clarified the biology of immunity and points to the solution of the transplantation problem. At present human individuality is the obstacle to spare-part medicine: the organism rejects grafts from other individuals, even though the alien tissue might be a life-extending kidney or heart. Why the chemistry of our cell membranes should be so individualized is not clear; it may impede the contagious spread of cancer cells, or perhaps of viruses which attack host cell surfaces.

There is little evidence of forethought about the social impact of the solution to the homograft problem, although this solution seems very near and may prove a prototype for the exercise of responsible power in biological engineering. Nor has the full impact of tissue replacement on the practice of medicine been

widely appreciated. For example, many therapeutic measures are at present barred or restricted by the possibility of damage to some organs in the course of therapy.

The medical revolution should begin to arouse anxieties over its orderly progress. We must recall that the homograft "barrier" has preserved the personality of the body. We have not hitherto had to think deeply about the technology and ethics of allocating precious organs for lifesaving transplantations. The potential dehumanizing abuses of a market in human flesh are fully anticipated in imaginative literature and modest proposals have been wryly recorded for the furtherance of international trade. Ultimately we must also reserve some concern for the identification of the person: what is the moral, legal, or psychiatric identity of an artificial chimera?

This is an alarmist and ungracious reaction to a gift of life. But we cannot overlook what medical progress has already done for the species in the name of humanity—for example, the catastrophic leap in world population through the uncompensated control of early mortality. We must try to anticipate the worst anomalies of biological powers. To anticipate them in good time is the first element of hope in developing institutional and technological antidotes. Only preliminary suggestions are possible, but even imperfect ones may help to illuminate the possibilities:

(1) Accelerated engineering development of artificial organs, e.g. hearts, which may relieve intolerable economic pressures on transplant sources.

(2) Development of industrial methodology for synthesis of specific proteins: hormones, enzymes, antigens, structural proteins. For example, large amounts of tissue antigens would furnish the most likely present answer to the homotransplantation problem and its possible extension to heterotransplantation from other species. Structural proteins may also play an important rôle in prosthetic organs.

(3) A vigorous eugenic programme, not on man, but on some non-human species, to produce genetically homogeneous material as sources for spare parts. The technical problem of

overcoming the immune barrier would be immensely simplified if the heterografts came from a genetically constant source, the more so if the animal supplying the grafts could be purposely bred for this utility. At present the only adequately inbred mammals are small rodents.

(4) The formal registration of all organ transplants (with some stated exceptions such as blood, patches of skin and similarly dispensable parts that can pose no problems of availability). This would furnish more precise statistics on present efforts at transplantation and help assure an orderly evolution of the technique.

The first three of these proposals illustrate an important gap between academic science and its economic application which too often private enterprise is discouraged or inapt to fill, and which, unlike basic science, calls for detailed social planning.

Man's control of his own development, "euphenics", changes the means and also the ends of eugenics, as have all the preceding cultural revolutions that have shaped the species: language, agriculture, political organization, the physical technologies. Eugenics is aimed at the design of a reaction system (a DNA sequence) that, in a given context, will develop to a defined goal. But will culture stand still merely to validate the eugenic criteria of a past generation? And for a given end, the means will have shifted: the best inborn pattern for normal development will not always react best to euphenic control.

Should biologists give first priority to long-range eugenic concerns of human genotype, or to the gravely imminent issues of human numbers and phenotype: the allocation of intelligence, motivation and longevity?

When euphenics has worked itself out we should have a catalogue of biochemically well-defined parameters for responses now describable only in vague functional terms. Then we shall more confidently design genotypically programmed reactions, in place of evolutionary pressures, and search for further innovations.

Eugenics and euphenics are the biological counterparts of education, a panacea that has a longer but equally contentious

tradition. The troubled history of Utopian education warns us to take care in rebuilding human personality on infirm philosophy.

In our enquiry on man's future, the aims of human existence are inseparable from the power and responsibility for human nature. As biological technology dissolves the barriers around individual man and intrudes on his secret, germinal continuity, we must face the issue of a definition of man, taking full account of his psychosocial progeny. We now recognize genetic continuity in mechanistic terms as a nucleotide sequence—in due course this will itself be subordinate to the psychosocial machinery. (Our global experiments on human mutagenesis by chemicals and by artificial radioactivity are the crude, random initiatives.) What will then qualify "man" for the aspirations of humanistic fulfilment, apart from the other robots born of human thought?

COMMUNICATION: OTHER WORLDS AND OUR OWN

In illuminating the chemical mechanism of terrestrial life, molecular biology has completed Darwin's effort at a general theory. This coincides neatly with the technical realization of space flight and of radio astronomy. The challenge of planetary exploration has made us think more deeply about the general principles of earthly life. The prime questions of exobiology, life beyond the earth, concern molecular biology. Do the Martian organisms use DNA and amino acids as we do, or are there other solutions to the basic problem of the architecture of evolution?

How seriously the radio astronomers take the prospects of interstellar communication is hard to fathom. At any rate, there is nothing in biology to discourage the hypothesis of multifocal intelligence in the universe. We have not really thought very much about the problem of finding the *rapport* needed to establish the first contact. It is many times more costly to transmit than to listen, which can lead to a perplexing stalemate in these cosmic negotiations. Hopefully, this technological issue will ripen into a more sophisticated theory of communication

without convention which may have wider interest, as it may also motivate greater investment in the technology of message transmission.

The content of the communication has been least thought about. It might be the greatest help to understanding our own philosophy. How should we epitomize ourselves in telling our story to others? I do not doubt we should describe DNA and proteins, possibly the most arbitrary and unpredictable consequences of cosmic evolution. Technically, the periodic table of the elements would be easy to encode, and would establish chemistry as a context of discourse. But what then? As our presence at this symposium witnesses, man is a communicative animal and it may be some comfort to offer this instinct an infinite challenge.

One prospect may be alarming—that we receive messages that betray our own scientific backwardness. What could erode scientific creativity, so dependent on the delusion of something new under the sun, more than the knowledge that everything is already known but only our access to the oracle is imperfect and costly?

The topic of our symposium warrants other insights, the style and allegorical licenses of the artist; the *verifiable* statements that any scientist might make in predicting man's biological future are probably vacuous. I have been alarmed about my own credentials, which should include responsible appreciation of the relevant science. I could reassure myself that it would be the utmost of human capacity to assimilate a fraction of what others have already said on the same issues, that I was setting myself an impossible task to achieve any novelty of concept or statement. But in acquiescing to this fact do we not now see another image of man's biological future, his future as a scientist?

Today some scientists succeed in assuring themselves of currency in their investigative work, partly through self-delusion, partly through choice of narrowly delimited fields, partly through arrogant but sometimes justifiable assumptions about the incompetence of most of their colleagues, whose papers may

then lie unread. A typical weekly reminder list distributed in our department may include upwards of a hundred titles. It would be a more than full-time occupation to digest just this sample of science, and it takes a constant act of judgment to decide what to take time for. The useful output of scientific work has not yet been impaired by the density of "creativity space". In any case, society's return for its investment in science is so great that it cannot afford to hold back from an even greater, though possibly less efficient, allocation of its resources to science and technology. Whether the individual motivation for a scientific career can sustain the pressure on creative opportunity is a perturbing question. The situation is bound to be aggravated by the general increase in population and in the relative popularity of science, perhaps most of all by the sudden accession of the once underdeveloped nations to the main streams of world science.

The problem is compounded by the archaic clumsiness of our basic mechanisms of communication. Man's dilemma is the discrepancy between the size of his population and complexity of his institutions, on one hand, and his individual feebleness, measured as a data input rate of no more than 50 bits per second. The linguistics of the future may improve the technique of speech, or open other channels of communication for our daily needs. Meanwhile it is anomalous how inefficiently science has applied existing technology to tend to its own needs of communication. Incredible to say, within the present system only by chance could I in future discover comments that others might publish in criticism of this very paper. The phenomenon of science has only recently attracted the analytical interest that can help to expose such anomalies. Until it has gone much further we can only guess at their roots in personal and cultural psychology. They do lend support to the hypothesis of unconscious resistance to effective, and therefore perhaps disturbing, communication.

The changes in the scope of research have changed its quality. Research is the effort to add to *human* knowledge. The extent of existing knowledge was hitherto more readily discoverable:

contributions were less competitive, did not need endless persuasion and repetition to be heard; the challenge was the struggle with nature. The complication of science has made it inexorably more human—or should we ever have forgotten this limit to objectivity?

Man's future as a biologist surely depends on the rationalization of scientific communication. Society makes many demands on the energies of the global community of science. We must also take care to look to the preservation of our own future by the modernization of our own techniques for efficient but free expression.

The theme of this paper was to have been molecular biology, the transfer of information from one macromolecule to another. It has become an essay on communication, under the same logic by which man has evolved from substance to concept.

Eugenics and Genetics

DISCUSSION

Crick: I find myself in a difficult position as opener of this discussion, because I am not really a biologist—at the most I am a molecular biologist—and we are discussing here matters which are concerned with biology proper. However, I shall select some general points that seem to me to be of importance.

I certainly agree with what Dr. Lederberg has said about the extraordinary rate of increase in biological knowledge, particularly in some fields. What impresses me even more is the great lack of biological knowledge among ordinary people: the ordinary educated layman, and to some extent among scientists other than biologists. I also think it is deplorable that knowledge of natural selection is not taught properly in schools.

I don't want to say too much on the detailed points that Lederberg raised. I was amused by his dramatic picture of a black market in organs; this is a very real possibility which we shall have to face. It is difficult for us to see at this stage which of the techniques such as transplantation are likely to have a large effect: I think they are likely to take us by surprise to some extent. As for the impact of molecular biology, I agree with Lederberg that the practical possibilities of synthesizing or modifying the germinal material are very far in the future. I agree too that developments in our knowledge of embryology and of the higher nervous system are going to cause the major changes in the next few decades.

I agreed with practically everything Muller said, with a few small reservations. Let us take up this whole question of eugenics. It is possibly not an acute issue compared with other acute issues we have to face. Nevertheless I think that we would all agree that on a long-term basis we have to do something—

Muller was much more eloquent than I can be on this subject—and because public opinion on this subject is so far behind, we should start to do something about that now. I would therefore like to raise a number of questions of a more ethical nature. I do this with great reservations because it is my opinion, in spite of Sir Julian's eloquent arguments, that we really do not have a proper philosophical foundation for humanist ethics. Nevertheless, if we do not accept Christian ethics, or the ethics of some other religion, we obviously have to have some other guidance. These rather vague terms like "fulfilment" appear to be the best we can do, but I do not feel they are satisfactory.

I want to concentrate on one particular issue: do people have the right to have children at all? It would not be very difficult, as we gathered from Dr. Pincus, for a government to put something into our food so that nobody could have children. Then possibly—and this is hypothetical—they could provide another chemical that would reverse the effect of the first, and only people licensed to bear children would be given this second chemical. This isn't so wild that we need not discuss it. Is it the general feeling that people do have the right to have children? This is taken for granted because it is part of Christian ethics, but in terms of humanist ethics I do not see why people should have the right to have children. I think that if we can get across to people the idea that their children are not entirely their own business and that it is not a private matter, it would be an enormous step forward. If one did have a licensing scheme, the first child might be admitted on rather easy terms. If the parents were genetically unfavourable, they might be allowed to have only one child, or possibly two under certain special circumstances. That seems to me the sort of practical problem that is raised by our new knowledge of biology. But let me come down to practical measures, because I think what I have described is a bit extreme.

Lederberg and I have arrived independently at an idea (which I hope he does not mind me quoting) that the type of solution which might become socially acceptable is simply to

encourage by financial means those people who are more socially desirable to have more children (this is not the idea favoured by Muller). The obvious way to do this is to tax children. This seems dreadful to a good liberal because it is exactly the opposite of everything he has been brought up to believe. But at least it is logical. There are various objections: there will be people who, however much the tax, will have many children, but they may be a minority. It is unreasonable to take money as an exact measure of social desirability, but at least they are fairly positively correlated. Of course, it is perfectly clear that you could not take such measures, as Muller very rightly said, with public opinion as it is, and with the general lack of biological knowledge.

Now to come to Muller's ideas. Is it possible that his scheme is the best way to give this type of biological education to the public at large? If *some* individuals were allowed to choose the father in the way he suggests, this might make the population as a whole reflect on the social responsibilities of parenthood.

There are also legal problems. For example, should it be open to any individual to allow his spermatozoa to be stored, or would he need to have a licence for his spermatozoa to be put into storage? Secondly, there is the question of how *many* progeny of a given individual should be permitted. And surely, one must be licensed; this is at least as much a matter of public interest as having a licence to drive a motor car. Again, how much influence should society have in the actual choice of sperm donor? I think it is reasonable that, up to a point, the individuals concerned should have a choice. And one might also license the mothers for the number of children they can have. These are the sort of issues which these two papers raise.

I would like to raise one final possibility of the way things may go. If such practices were adopted, it might happen that one particular country would initiate a larger-scale programme than any of the others, and after 20, 25 or 30 years the results might be rather startling, if, for example, all Nobel Prizes began to go to, say, Finland because they had gone in for improvement

of their population on an extensive scale! If there are advantages in these techniques, and one society or nation does adopt them with marked success, this will accelerate adoption elsewhere.

But the real difficulty will be the lack of biological understanding of people at large; this will be an enormous handicap, especially in view of the tremendous rate of progress in biology which we expect to see in the next 20 or 30 years.

Koprowski: Could I very briefly take up two questions Dr. Lederberg raised about the transplantation of organs? They are (1) the production of transplantation antigens from human tissues and organs in large amounts for conditioning to homotransplantation and (2) the availability of tissue transplants in large quantities.

I believe that transplantation antigens can be extracted from human organs and tissues, which can be preserved by creating "banks" of frozen tissues. The extraction of sufficient amounts of antigen (which does not need to be chemically pure) will be greatly facilitated by the fact that tissue culture systems provide us with facilities for making available almost unlimited amounts of human tissue revived from the frozen state.

The availability for future generations of "ready-made" transplants of intact human organs such as heart or kidney may present a much more formidable problem. Perhaps, following the current use of plastic heart valves and arterial walls, it will be possible to construct plastic prostheses of heart or kidney which would be accepted by the human body and remain functional in it.

Medawar: I agree with Dr. Lederberg's remarks on the possible social dangers of replacement therapy. I have thought about them myself, and I think the reason why I haven't called public attention to them is simply because one is apt to thrust these rather unpleasant things out of one's mind. But I agree with him in general, and also with what he said in particular about possible solutions of the problems of transplantation.

Pincus: I would like to take up one of the questions which Dr. Muller left unanswered: that is, if you are going to consider

the use of sperm or egg banks, you must know whether or not the preservation of germ cells at low temperatures has an effect on the rate of mutation. So far we do not know anything about mutation rates at extremely low temperatures. That is something that must be settled before we can donate sperm to be kept for generations.

In addition to the preservation of eggs or sperm, there is the possibility of preservation of the generative tissues—the testes and the ovaries—particularly, as Muller points out, in the embryonic stage. If we could take tissue containing embryonic germ cells, preserve it for long periods of time, and transplant it to useful recipients, we might have a source for future breeding which could offer a chance for survival of spermatogenic tissue in particular for much longer than now seems possible.

Dr. Muller has not discussed in his paper the possibility of breeding by parthenogenesis, that is, reproduction from the unfertilized egg. This has numerous advantages over artificial insemination, particularly the possibility of attaining a purer strain (homozygosity) in a relatively short time, whereas if you are going to use selected sperm as a means of reaching any desired degree of homozygosity, you have a long way to go. Intensive application of research efforts to this problem of parthenogenesis should be very profitable.

Hoagland: Hasn't it been shown in the fruit fly, *Drosophila*, that the mutation rate increases with temperature and is lower at lower temperatures?

Haldane: Yes. In addition, somatic mutation in some plants has a negative temperature coefficient.

Koprowski: The effect of preservation at low temperature on mammalian cells may be related to the type of tissue and the species of origin. We have considerable data indicating that some human embryonic cells (fibroblasts) retain their genetic integrity in the frozen state but we do not have any information about epithelial-like cells. It is also possible that freezing favours selection of the fittest cells, namely, those that have the best growth potential. These may "throw off" mutants at a

greater rate than other cells, particularly if obtained from a "genetically labile" animal species such as hamster.

Crick: If you are going to store germinal material for any length of time, it is absolutely essential to see whether there will be any deterioration, and this should be investigated as soon as possible. On theoretical grounds, many types of mutation would not happen at very low temperatures; others might. I don't think it is fair to apply to sperm the arguments used for other cells, because the sperm head is packed in a particular way, and the sort of damage you might get in low-temperature storage of other cells might not necessarily occur in spermatozoa.

Koprowski: Could the results of artificial insemination of animals with frozen semen be applied directly to man?

Crick: If something works with animals one is more confident, but not completely confident. But this should certainly be worked out extensively with animals.

Pincus: Large numbers of bull calves have been born after artificial insemination from frozen semen and there has been no evidence of an increase in the mutation rate. However, if mutation to *recessive* lethals occurred, it would not show up in the first generation, and I do not know of many studies beyond the first generation.

Hoagland: I might mention that we have worked with what was perhaps the first human sperm bank. In 1940 Pincus and I showed that if human sperm were dropped into liquid nitrogen, they could then be revived if one warmed them up very quickly; 60 per cent of them were motile even when they had been kept for indefinite periods of time with dry ice. We could not vitrify and recover sperm of domestic animals to any significant extent. Human sperm are quite exceptional in this respect. Storage of animal sperm did not become practicable until Parkes and his group developed a method using glycerol as a protective substance in freezing.

About this time I wrote a rather facetious article in the *Scientific Monthly* pointing out that women might have offspring by selected long-dead donors; they could perhaps choose the

equivalent of a Shakespeare, a Newton or even a Rudolph Valentino to father their offspring.

Medawar: I think the question of freezing sperm is irrelevant to the eugenic principles that Muller is trying to propagate. The reason why he has now adopted the idea of preserving sperm is to meet the criticism justly made by Dr. L. C. Dunn, that Muller himself has changed the composition of the select list of sperm donors whom he would choose to father a high proportion of succeeding generations. As Muller's opinions have changed, so the list of preferred donors has changed. This is only one of many objections to Muller's scheme.

Klein: Muller has certainly changed his opinions; twenty years ago, in his book *Out of the Night*, he asked: where is the woman who would not be eager and proud to have in her womb a product of Lenin or Darwin? I don't think Muller would put Lenin and Darwin together now.

Huxley: The point about deep-frozen sperm is surely that it is a technical device to secure multiple, and therefore quickly effective, selection. As for Muller changing his mind, I think he has changed it in the right direction. He has left the choice now, I think rightly, to the parents themselves. What we ought to do is to plant "Seeds of the Future" in this field—a few experiments in which parents would be able to choose the donors for their children. At present, I understand that in artificial insemination by a donor the parents are not allowed to know who the donor of the sperm is. Donors should all be registered and parents should have a possibility of choosing. This could be extended to a multiple choice system.

Dr. Pincus said that it would be easier to get homozygosity by parthenogenesis. But do we want homozygosity? As a eugenist, I certainly don't. Surely the hybrid vigour, due to heterozygosity, of the human species is highly important, and there is no reason why one should not get general improvement in the level of various desirable characters without fixing any one of them, as you try to fix characters in a breed of dogs.

Haldane: I agree with Muller when he said that in most existing societies effective fertility is negatively correlated with

social rank. The same observation was made approximately 2,000 years ago in the statement "Blessed are the meek for they shall inherit the earth". It is possible that this is not an entirely bad thing, because the bad qualities of people who achieve social prominence in the human societies of which we have record are quite as striking as their good ones. Obviously you need a certain amount of ability for this, but you may need some other qualities which are not as desirable. I think that this "meek inheritance" does apply on a larger scale. If you resist invaders, provided you do it sufficiently well, you may survive, but otherwise you will be massacred. The people whose ancestors have never offered much resistance to invaders, such as the Gujeratis in India, seem to have survived in considerable numbers. Similarly the West African negroes have been sufficiently meek to propagate as slaves, and survived, while the Caribs, for example, did not. I think we have to consider such points as these before we regard social approbation as necessarily desirable from the point of view of what we want in the ultimate future.

I think most of Muller's ideas are entirely acceptable to traditional Hindu thought. In Hindu law there are approximately 12 categories of sons: it is much the best to have your own sons begotten on your own wife; and in about the third category are those begotten on your own wife by someone appointed by you—they are much better than those begotten as a result of seduction or rape. I do not think that among people with the Hindu tradition you would find the resistance to such ideas which you would in some other traditions.

My own view is that what Lerner calls "genetic homoeostasis" makes it much harder than seems likely at first sight to produce the results which you wish by selection, unless it is something comparatively trivial like the colour of an egg-shell or of hair. Anything even as complicated as the qualities of a good laying hen is very much harder to fix by selection than was considered earlier. I am afraid we might find the same thing with human characters, until we know something about the genetics of the desirable ones—which in my opinion we hardly do.

Klein: As a professor of biology, I agree very much with Dr. Crick that there is a tremendous rate of increase in biological knowledge and a lack of biologically educated people, at all levels of education. But there is always the risk that biology will not be taught objectively. We have an example in the biology taught in Germany during the Hitler régime. There were books on biology for all levels of education, but it was *directed* biology. This emphasis on biology was apparent even in the law: there was a long biological introduction by Professor Rudin to the law on eugenic sterilization passed in July 1933. We must be very careful in teaching biology, and especially in teaching eugenics, not to teach a directed biology like that of Muller.

Huxley: The answer to this point is that we must let the biological profession itself do the job of improving the teaching of biology. In America, a committee of the American Institute of Biological Sciences, originally headed by Bentley Glass and now run by Grobham at the University of Colorado, has already prepared three parallel textbooks and sets of teaching aids for high school biology[1]. They appear to be most successful in giving the high school boy or girl a good understanding of biology as a whole in a remarkably short time. I understand that the Gulbenkian Foundation is doing something of the sort in this country.

Pirie: I would argue that, within limits, bad biology is better than none. The place to start is surely with the Cabinet. I would be very much happier if I thought that those who govern us knew the rudiments of biology.

Taking up Crick's point about the humanist argument on whether one has a right to have children, I would say that in a society in which the community is responsible for people's welfare—health, hospitals, unemployment insurance, etc.—the answer is "No". I should like to hear what Coon has to say to the proposition that people do not have an innate impulse to have children as opposed to the innate impulse to have fun. What has always appeared to me the ideal contraceptive technique would be a situation in which people would normally

be infertile and should do something if on any particular occasion they wished to become fertile. If such a method were available, how much trouble would it cause in a community once the idea had penetrated? I think that most of the impulse to have children is a cultural one, built up by the kind of stories you read, the kind of pictures you see; I do not think it is a basic impulse at all. The impulse is sexual and that is the object people are pursuing—the children are inadvertent.

Coon: I think that they want both sexual pleasure and children. This business of women wanting to have children can become overpowering; I think there is a hormonal basis for that. I do not believe that the reason is purely social. This impulse is generally more important to the woman than to the man, but it can be very important to a man, too.

Comfort: May I take issue with Pirie? He says that people do not have the right to produce children. I would think that it is more true to say that whether people have the right to produce children depends on the circumstances. What I am sure of is that no other persons have the right to prevent them, which is rather a different matter. Hearing Crick speak reminded me of a calendar which you can see in workshops in the north of England representing a very male bolt pursuing a very female nut which is remarking to him "Not without a washer!" It is open to the female to say "not without a washer"—the reference is to a wedding ring, no doubt—but not to the government. I personally feel that even in circumstances where it would obviously not be a good idea to have too many children, we should be obliged to foster resistance to any governmental attempts to dictate whether we should or should not have children or which of us should do so.

Trowell: I think the traditional Christian ethics give one clear guidance on these matters; they stress the importance of the family group, physically and in every other sense. If one rejects these ethics, as many have done, then I think one must question whether a woman has the right to choose the inheritance of her child. On a purely humanistic basis are we not designing for the future of the race? We may have to say that a

particular woman is not suitable to have any children and another woman is only suitable if linked with certain specified spermatozoa. One would have to decide which spermatozoa, not just which men, were best. The fundamental unanswered question would then be—for what values are you going to breed? What is there to stop a totalitarian country breeding for efficiency, even cruelty and the absence of a moral and social sense? Is not this the logical outcome of breeding for a humanistic concept of survival and progress? If that is our aim one cannot leave these matters to the individual.

Crick: I believe that basically society has the right to decide, but what techniques can our society use to impose this to a reasonable extent (not necessarily to 100 per cent), without incurring some other costs? The proposal of licensing that I somewhat playfully suggested might, or might not, be acceptable in our present social system. The question that was just raised as to whether there is a drive for women to have children and whether this would lead to disturbances is very relevant. I would add, however, that there are techniques by which one can inconspicuously apply social pressure and thus reduce such disturbances. After all, we already have social forces which make us limit in one way or the other the size of our families. So although it may turn out that society has the right to determine who should have children, and in what way, the actual technique to be used has to be judged against the background of a social complex including the amount of education. This is why I think biological education is so important, because it enables the solutions to be attained with less stress to the social system.

Coon: Adoption of children sometimes seems to fill the bill so far as the maternal urge is concerned: plenty of women have a tremendous maternal urge which is satisfied perfectly well with someone else's children.

Crick: That is a very good example of how one could get round one of these problems.

Bronowski: I find myself out of sympathy with much that has been said in Muller's and Lederberg's papers. That is

because I really do not understand what problem you are trying to solve. If you are trying to upset violently the present gene frequencies in the population, then nothing that Muller proposes could do this. Just as Haldane has shown long ago that sterilization of the unfit would hardly have any influence on the proportion of recessive genes, so the multiplication of what we choose to call the fit can really have very little effect on the presence of recessives. (And no one who has known the children of accepted geniuses would suppose that the population would greatly benefit by there being several hundred of them.) If you are trying radically to change the gene frequencies, of course you can only do that in Crick's way, that is by forcibly preventing all but a few genes from reproducing. Even this supposes that you know (a) why you think a particular gene is good, and (b) what tests to apply in order to identify it.

However, I took Crick's remarks to be a *reductio ad absurdum* of the method of direct control of the gene frequencies. Indeed, we might achieve the same effect in a simpler way—by eating the children of the unfit, as Jonathan Swift suggested that the Irish poor should eat their own children. But what problem are we trying to solve? What genes are we trying to boost? Muller asserts in his paper that there are reasons to believe that the human population is deteriorating, and Huxley in one phrase in his paper also implied this. I know of no evidence for that. I know of no evidence that the present human population is inferior, in any respect that one could quantify, to the human population 50 years ago. On the contrary, the only important experimental test of this assertion—the experimental intelligence testing of Scottish children which has been carried out over the past 25 years—produced exactly the opposite results. The human race seems to be improving itself by those natural means which I propose to continue to enjoy so long as I can!

MacKay: I have been thinking of Shaw's mischievous remark: "What has posterity done for me that I should do anything for posterity?" Since the relation between individual responsibility and that of "society" is in fact still unclear, the notion of "our" responsibility to tinker with the genetic

composition of posterity is doubly obscure. Without a much deeper analysis, the unguarded transfer to "society" of ideas proper to individual responsibility can mislead us into talking —and selling—moral nonsense.

That such nonsense has proved saleable, especially in Nazi Germany, should warn us against evaluating our plans for the race solely in terms of technical feasibility. We should, however, note one technical snag in any proposal to make the human genetic constitution self-regulating. I mean the difficulty of preventing the "goal-setting" from drifting or oscillating as time goes on, under the influence of external or even internal factors. Suppose, for example, that "we" (biologists? or politicians?) decided (and had the power) to make the next human generation of type "X". So far, perhaps, so good. But when we die, our place must presumably be taken by a new committee—which would presumably be of type "X". The question we must ponder is what kind of changes these men of type "X" would think desirable in their successors—and so on, into the future. If we cannot answer it, then to initiate such a process might show the reverse of responsibility, on any explication of the term.

In short, to navigate by a landmark tied to your own ship's head is ultimately impossible. If we are ever to make proper use of our growing eugenic powers, we shall need a wisdom greater than our own.

Here let us be quite candid. There is little agreement today that such wisdom is available, let alone as to its origin. But I believe strongly that this does not make discussion at this level pointless or impossible. For the beginning of wisdom is to ask the right questions; and it is by each faithfully drawing attention to—and listening to—questions which from a different viewpoint might not be raised, that we can most fruitfully co-operate for human welfare.

Brock: I would like to echo Bronowski's question: What is the problem that Crick and Muller are trying to solve? And are they thinking about some other problems which would arise out of the solution of what they think they are trying to

solve? Are we going to bring to humanity the happiness which undoubtedly we all want? Sir Julian asked the question: What are people for? I don't believe that any of us really knows the answer, but I suppose that self-expression and self-fulfilment must be among the objectives of mankind. This brings me to the psycho-emotional aspect of the woman who is denied children. Even where childlessness is inevitable, even when she is married to an impotent husband to whom she is devoted, the psycho-emotional effect of this situation on her is devastating. Admittedly the need to have children can be met up to a point by adoption, but not when there is another alternative. In my opinion no woman is going to be emotionally satisfied by the adoption of children, when she knows that she could have had children by her own parturition. If we are to have a healthy society, we must have a society in which such psycho-emotional upsets are reduced to the minimum. When it comes to the solution that Muller proposes I doubt that, even with improved biological education, many men will be emotionally satisfied by children not their own, if they are also able to have children in the normal way. And without this emotional satisfaction and fulfilment I doubt that we would have a healthy society. There may be a small group of "advanced" or otherwise abnormal people who would be satisfied, but the average man in my opinion would not be. I agree with Pirie that perhaps for many men it is the fun rather than the children that they desire, but this is not true of all men and is certainly not true of the average woman.

Trowell: Speaking as a physician, I should like to emphasize the very profound psychological effect on both men and women who cannot have progeny by the natural method. It has played havoc with many of my patients and some of my friends.

Klein: I agree that the psycho-emotional reaction of a man who cannot have children is very strong. There are a number of married people who have no children because although the man is potent, he is sterile; this is a most unhappy situation and it is very difficult to explain to a couple that a man can be both

potent and sterile. I think more research is needed on the problem of sterility in the male.

If we ever adopt Muller's techniques, we shall have to have biographies, not only of the great man whom we are considering as a sperm donor, but also of his antecedents. However, the present state of our knowledge of human inheritance is extremely fragile. I think we are still at the beginning of the study of human heredity, and before applying it I feel we must know it much better.

May I finish with a story by the German biologist, von Uexküll, about a man who discovered his own shadow. This man came to believe that his shadow was a living thing. At first he imagined his shadow to be his servant, because it copied all his movements; but he gradually began to doubt this and to believe that he was imitating the shadow. Thereafter he showed more and more consideration for his shadow, allowing it to have his seat or bed while he himself remained uncomfortably to one side. This man was eventually reduced to being the shadow of his shadow. Perhaps we also are too conscious of our shadows and forget what we are ourselves.

Lederberg: In answer to Dr. Bronowski's question about our motivation, I think that most of us here believe that the present population of the world is not intelligent enough to keep itself from being blown up, and we would like to make some provision for the future so that it will have a slightly better chance of avoiding this particular contingency. I am not saying that our measures will be effective, but I think this is our motivation; it is not the negative but the positive aspects of genetic control that we are dealing with here.

On the other hand I have serious doubts about the proposals for controlling reproduction that have been presented to us. The aspects of *social* control that seem to be necessary to make these proposals technically effective are I think extremely offensive and extremely dangerous, certainly in our present social context. But leaving the matter to individual choice, which from a social standpoint is the most ideal, is certainly not going to be technically effective. And if people are allowed to

choose the fathers of their children, will they not choose just the more notorious projections of their own images, exaggerated by the publicity given to advertised donors?

Comfort: Dr. Lederberg, what makes you think that we could make ourselves less likely to blow ourselves up by a genetic increase in intelligence?

Lederberg: I didn't say I thought we would succeed; I said I think this is our underlying motivation for attempting genetic control.

Comfort: I should think that it is not so much low I.Q.'s, but personality problems and emotional disturbances which were the cause of our liability to blow ourselves up.

Lederberg: These are just as likely to be under genetic control.

Comfort: They may be, but in man there is a large latitude for training. Dr. Trowell spoke about breeding a generation that displayed cruelty and efficiency. I think one could do this—or for that matter do the opposite—much more simply by *upbringing* than one can by trying to alter genetic constitution.

Bronowski: I would still like an answer to my question. What is the evidence that genetically the human population is deteriorating?

Huxley: The evidence is mainly deductive, based on the fact that we are preserving many more genetically defective people than before, and are getting a lot of radioactive fallout. Meanwhile, the study of intelligence in Scottish children which you cited is not valid evidence. During the period between the first and the second tests, children generally were becoming larger, were developing more rapidly, and therefore were becoming more intelligent for their chronological age.

The important point, however, as Lederberg said, is not the negative one of deterioration (although it might become so if there were greatly increased fallout); the main thing is to aim at positive improvement. Much is possible and there are methods to do it. You need not start with drastic methods; nobody is going to solve the population problem by saying that a certain number of people are not going to be allowed to have

any children. But you can make a start. At the moment many governments are encouraging people to have more children than they otherwise would by means of high family allowances. Why shouldn't you start by regulating family allowances, so that parents get a lot of money on the first two children, say, then less for the third, and then tailing off rapidly to a negative payment, a deduction, for children above a certain large number?

But the basic point was raised by MacKay, that you will have to nail your colours to some moral mast. In the present state of the world you will have to find a new moral mast to nail them to, and this will only come about by more knowledge and more education and more thinking; and this is a feedback process. At the moment the population certainly wouldn't tolerate compulsory eugenic or sterilization measures, but if you start some experiments, including some voluntary ones, and see that they work and if you make a massive attempt at educating people and making them understand what is at issue, you might be able, within a generation, to have an effect on the general population. After all, our moral values evolve like everything else and they evolve largely on the basis of the knowledge we have and share.

Glikson: Like Dr. Bronowski I do not see why we need the application of biological technology in changing the quantitative and qualitative composition of whole communities or of humanity. But I think emphasis should be laid on the dangers involved in the very development of such biological technology, because its application would most probably fall into the hands of political forces which would use it for quite different purposes than those anticipated here. Biological technology as explained by Lederberg, Crick and others here effects a one-sided manipulation with individual and social life. Such developments must to my mind be accompanied by some control. Where interference seems desirable, it must be guided by a sympathetic and comprehensive view of human and environmental evolution. Such control might be achieved by co-operation not only among scientists, but among the best

scientific, imaginative and idealistic forces of the world community forming "composite minds".

Price: I would like to go further than Bronowski, and suggest that the psychosocial system might in its own bumbling homoeostatic way actually be doing the right job. We know that a great deal of the performance of man depends as much on social environment as on genetics, and this environment might act in a way completely opposite to that which would be produced by the mechanisms of genetic control which we might introduce. For example, creativity, intelligence, and the leaning towards science are apparently, on the basis of historical evidence, enormously helped by such things as being first or only children, and by losing a parent before the age of ten; these things together improve your chance of being a good and creative scientist by something like a factor of ten. Now, if the better people are having small families, they are increasing the frequency of only children, thereby giving their group an increased chance of success; and to increase the number of people carrying these genes by encouraging larger families among the more intelligent people might be to deny the possibility of the very environment which would let these factors work.

Pincus: I am very surprised to hear some people here say that genetics has taught us nothing about nature and that if we breed in a random manner by the old-fashioned methods, we shall get good genes. This is nonsense genetically: you don't get good genes by breeding in random fashion; you get good genes by selection. If, however, you want to emphasize the phenomenon of heterosis or hybrid vigour, as Huxley has done, and argue that the real reason for the success of the human race is that there is so much interbreeding that you are always getting heterosis phenomena, then I accept that you have an argument there. But if we are talking about *genetic* improvement, you have to select good genes.

Trowell: Could I put in very briefly the point of view of the Roman Catholic church (speaking as someone who is not a Roman Catholic and who does not subscribe completely to

that point of view)—their great emphasis on natural law. I think they would say that we should be very careful before we distrust what has worked for about a million years in the human species and for longer than that in the animal creation, for this is one aspect of natural law. In this connexion, I have never understood how the human race got over the biological hurdle of moving from polygamy to monogamy. Under the polygamous system the favoured and cultured person, the king or chief, sires a large number of people in the community, and under those conditions we ought to have intelligence building up more rapidly than under the conditions of monogamy. As far as I understand, the human race was polygamous for the best part of a million years, whereas it has been monogamous in varying degrees of stability for a very short period of time. Until somebody can demonstrate to me how we have abolished polygamy and still progressed I shall be sceptical about any new changes. I hope none of my remarks will be taken to mean that I dissociate myself from what I understand as the Christian ethics of these matters.

Haldane: I made that point some 25 years ago by pointing out that according to many eugenic articles a Turk should always get the better of an Armenian or a Jew in a business deal.

Huxley: *Ceteris paribus!*

Clark: Dr. Trowell used the phrase "natural law" in the sense of something which has been going on for a very long time. I would define it differently; it may coincide with what has been the practice of mankind or it may not. Several people have raised the question of what is the purpose of man on earth. I feel a bit hesitant at entering this field and would have preferred a professional to have tackled it—but the main purpose of man on earth is to love God and obey his commandments. I know that poses a difficulty for people who deny God's existence but I think they ought to take a look at this view, and consider how other conclusions follow from it. Cultural fulfilment and enjoyment are secondary purposes in man's existence, not his primary purpose.

One of the primary commandments is to respect the rights of others. I think that this is the point where the humanists may be able to rejoin the Christians. There is a widespread tendency to fail to respect those rights, or to fail to define them properly. These rights are quite numerous: the right to earn a livelihood (economic rights), the right to marry, the right to beget children—that is clearly part of natural law—and at the same time the duty to look after them, and not throw the responsibility on other people.

I am rather surprised at the extraordinary concern which is shown here about contraceptives, even by people who feel very strongly that they are entitled to use them, because it seems to me a little out of date now that so much more is known about how short the period of fertility is in the menstrual cycle, and the possibility of regulating the menstrual cycle where it does turn out to be irregular. I understand that moral theologians say that taking a medicine for the purpose of regularizing an abnormal cycle is not an offence against natural law (using the word in the moral sense), whereas to take a pill for the purpose of rendering yourself infertile is. I think that this is clear. Now that knowledge has been acquired and is spreading about how very short the fertile period is, a great many Roman Catholic clergy and laymen are extremely anxious for population limitation and they regard my views on population as extremely harmful; one very prominent French priest has complained strongly that the things I am saying about the agricultural capacity of the world are hindering his campaign to make marriage more spiritual by producing fewer children. This is a theological matter on which I should not seek to express an opinion, but I do want to point out that opinion among Roman Catholic clergy and laymen is considerably divided on the question of the desirability of increased population.

Coming back to questions of morals: artificial insemination by a donor other than the husband has all the malice of adultery —it is a form of adultery—and I think that anyone who understands the moral meaning of the word adultery is bound to reach that conclusion.

As for eugenics, it is still true, as it was fifty years ago, that while knowledge of human genetics has improved, it is still very limited. Eugenics has been through its first cycle—it started with extremely brilliant, rather unscrupulous scientists of the type of Karl Pearson, and popularizing humbugs of the type of Saleeby, and in the Edwardian decade it was intellectually fashionable. I think that this first cycle of eugenics never recovered from the witticisms of Haldane and Hogben—Haldane in the more classical, Hogben in the more popular manner. It is just as well that it did die because we have seen in Nazism where it may lead. I think that it is no accident that the Nazi doctrines about sterilization were closely linked, intellectually and morally, to Nazi doctrines about genocide. That is why I am so alarmed to see what is happening today. Apparently we are beginning a second cycle of eugenic doctrines supported by some brilliant and misguided scientists, and which I am afraid will attract its quota of humbugs as well.

Crick: I disagree strongly with Dr. Clark's remarks and with the standpoint from which he made them. It is clear that if we take the broad ethical question of ultimate ends we shall never reach any agreement. Moreover, those of us who are humanists have a great difficulty in that we are unable to formulate our ends as clearly as is possible for those of us who are Christians. Nevertheless there are some ends that we can all share, even though we have these differences. It is surely clear that good health, high intelligence, general benevolence—the qualities Muller listed—are desirable qualities which we would all agree on. We would agree also that these qualities are not uniformly distributed. There are people who are deficient in intelligence, for example (I mention intelligence because this is something we can to some extent measure). Surely it is a very reasonable aim for us to try to increase that. Some of the arguments that "nature is doing it all right" may possibly be correct but they seem to me only to reflect conservatism and to have no real basis of fact. We are now in an environment that is changing very rapidly, and has been changing for the last few thousand years, but we evolved, as was

made clear by Muller, over a much longer period of time in very different circumstances. Consequently, we should not *necessarily* go on as we are.

Are the methods for improvement which we have at our disposal effective? Now there are difficult technical questions here, but my point, which Huxley made rather strongly, is that we are likely to achieve a considerable improvement—not perhaps as fast as we could do by other methods or even as fast as may turn out to be necessary—by using a very primitive knowledge of genetics; that is, by simply taking the people with the qualities we like, and letting them have more children. Nobody is suggesting, at least it would be foolish if they did, that we should have *enormous* numbers of people all with one father; one should have a wide selection of donors and so get diversification. The difficulty I see concerns the techniques that are *socially* possible, in the present social context, and in the social context of the next twenty or thirty years—a context which will change and which to some extent our views may help to change. For example, psychological problems may arise in families with children who are not the children of the father. Whereas I reject utterly arguments about natural law, I am much concerned that evidence on the psychological problems in such families should be collected. We already have examples of families where the father is infertile and the mother has had a child by artificial insemination by a donor; I understand that the disturbance to family life is often not great in such cases. I agree entirely with Huxley that what is wanted here is some sort of limited programme to try and find the difficulties. Let us define our broad aims and then tackle the practical details.

Medawar: I agree with a good deal of what Crick has just said, but I think we ought to be warned by the very diversity of opinion in this room. We all have a pretty good opinion of our own intellect and our worthiness to be sperm donors. But our opinions are extremely diverse, and my feeling at the moment is that human beings are simply not to be trusted to formulate long-term eugenic objectives—least of all Roman

Catholics. What frightens me about Muller and to some extent Huxley is their extreme self-confidence, their complete conviction not only that they know what ends are desirable but also that they know how to achieve them. I can perhaps imagine approving of the kind of scheme Muller has outlined if he put it this way: "we don't really know a great deal about human inheritance but with the co-operation of a number of volunteers let us put my scheme into practice and perhaps we shall learn from it".

Huxley: But surely Muller's point, and certainly mine, is not to think in terms of any definite eugenic ideal; the aim that I have in mind is the very general one of gradual improvement.

Medawar: But you don't know how to do it! May I challenge you to explain Evelyn Hutchinson's paradox about homosexuality? The proportion of homosexuals has probably not declined over the period of recorded history; yet according to all selection theories which we are so confident about, the proportion should have declined on the reasonable grounds (a) that homosexual tendencies are to some extent genetically determined and (b) that homosexuals are on the whole less fertile (even if fractionally less fertile) than normal people. It follows that the genetic endowments that make for homosexuality or parasexuality in general should have declined. In fact they have done nothing of the kind. This means either that so deep-seated a trait as parasexuality or homosexuality is not genetically determined or that we don't really understand the mechanism of its inheritance.

Huxley: I didn't know about this paradox, and am afraid I can't answer that point. In any case I want to look at the problem from another angle. You say we must know more about the details of human genetics before we can think about improvement. I really don't see why. Darwin knew nothing about the details of reproduction, still less about genetics, and yet he was able to deduce a set of principles and a general theory of evolutionary transformation which have stood up to the test of time. Our new knowledge is merely permitting us to fill in the details and add a few minor modifications. What I

want to stress is that if we can find the right method of exerting selective pressure, we could make for human genetic improvement. We must do it by way of experiment.

Dr. Trowell talked about breeding for efficiency. This is very important because, as psychosocial organizations get more and more complicated, we need more and more good brains at the top to run them. If you assume as a first approximation that intellectual efficiency or intelligence has a strong genetic component, and that it is distributed according to the ordinary type of symmetrical frequency curve, you can calculate that a very small increase in the mean will produce a large percentage increase in the upper values; so far as I remember, if you could raise mean I.Q. from 100 to 101·5 you would raise the percentage of people with an I.Q. of 160 and over by nearly 50 per cent. The increased social and cultural efficiency resulting from a small difference in the number of outstandingly gifted people is also very important in considering the problem of possible racial differences.

Lederberg: The converse of Huxley's calculation is that in order to shift the mean I.Q. by 1·5/100 you must increase the production of geniuses by 50 per cent. It is perhaps better to aim at just increasing the variance. The question is not whether we should think about doing eugenics; we certainly should, and should collect just as much information as possible. The point is whether we should embark on a concrete programme that is very costly in social and political stresses for an aim which isn't very well crystallized yet.

Huxley: I think most people would agree that even if we cannot yet carry out a eugenic programme, we can begin doing something about controlling the quantity of population. The experience we gain in this field will help us to deal with eugenic problems later.

MacKay: I agree with Crick about the "weakness" of saying that the system is probably working as well as it can now; but is it any less logically "weak" to say "maybe this and that remedy will be better"? A good example is this question of increasing I.Q. Is it obvious that the psychosocial structure,

whose intricacy is as yet unknown, will not be harmed more than helped by such a change? For example, most criminals now are rather stupid. Are we quite sure that by raising the I.Q. of the population all round we won't create new problems by increasing the brightness of the average criminal? All sorts of complex factors are involved. If any one of us had devised a mechanism as complex as the situation of the human race, how would we feel about letting any of our colleagues monkey about with it, on the assumption that they knew as little about it as we know about the psychosocial mechanism?

Comfort: I still feel a little despairing at hearing this gathering continue to confuse intelligence with what I would call adjustment in personality. We wouldn't do at all well with a population consisting solely of people with a very high I.Q. who were also maladjusted or even psychotic.

Potentialities in the Control of Behaviour

HUDSON HOAGLAND

A SCIENTIST operates under the tacit assumption that there is order underlying the phenomena he is studying, otherwise his work would be pointless. He hopes to find the nature of this order. He also assumes that all forms of order have determinants and his job is to discover them. If he is studying behaviour of either animate or inanimate systems, he seeks the mechanisms of that behaviour. Since all natural phenomena, including the behaviour of living organisms, are subjects of successful scientific investigation, the assumption that events are determined by antecedent conditions and by environmental factors has been empirically justified by the success of science, especially over the last three centuries. I know of no scientists who work today outside a deterministic framework.

Considerations of the age-old mind-body problem and of the nature of mechanisms, of purpose and of freedom have undergone modifications over the last century, especially in recent decades, and these considerations are relevant to reflections on human behaviour and its control. Thus, to quote Julian Huxley[1] "The only satisfactory approach to the mind-matter problem is the evolutionary one. Let us begin with human beings. We are organizations of—do not let us use the philosophically tendentious word 'matter', but rather the neutral and philosophically non-committal term translated from the German *Weltstoff*—the 'world stuff' of which the whole universe is made. We then are organizations of world stuff, but organizations with two aspects—a material aspect when looked at objectively from the outside, and a mental aspect when experienced subjectively from the inside. We are simultaneously and indissolubly both matter and mind." Huxley considers the possible evolution of

mind from simple organisms to man and its survival value by natural selection. He continues: "What is the function of mind? Why did it evolve to increasing heights of intensity and importance? What is the biological value of the mental aspect of life in higher animals? It is now certain that natural selection through the differential reproduction of genetical variants is the essential agency of directional change in evolution. This being so, mind cannot be a useless epiphenomenon. It would not have evolved unless it had been of biological advantage in the struggle for survival. I would say that the mind-intensifying organization of animals' brains, based on the information received from the sense-organs and operating through the machinery of inter-connected neurones, is of advantage for the simple reason that it gives a fuller awareness of both outer and inner situations; it therefore provides a better guidance for behaviour in the chaos and complexity of the situations with which animal organisms can be confronted. It endows the organism with better operational efficiency."

Ideas about the nature of mechanism have changed from those of the nineteenth century. The principle of negative feedback, whereby energy released from part of a system returns to regulate and control further energy release by the system, is the basic principle involved in cybernetic mechanisms. Examples include engine governors, the thermostat that regulates the heating of a house, and the guided missile that bounces its own radar waves back from the target and uses this feedback to regulate its steering and power to make it home on target. Computers have a remarkable complex of feedback processes including the utilization of information storage and its appropriate retrieval, which corresponds in us to memory and recall. Purpose can be defined in terms of mechanisms controlled by negative feedback; purpose so defined is built into the guided missile and the computer and the thermostat, enabling these mechanisms to accomplish ends of varying degrees of complexity. Problem-solving computers can play a good game of chess, translate one language into another, and improve their capacity to discriminate as a result of past experience, i.e. to learn.

Objection has been raised to calling such mechanisms purposive, since their purpose has been built into them by man. But man himself and his behaviour are the result of purely fortuitous mutations acted upon by natural selection. Natural selection that has produced purposive human behaviour is itself a non-purposive process.

Whereas feedback devices of control have developed rapidly in engineering in the past twenty years as a product of social evolution, biological evolution by natural selection brought such mechanisms to a high order of development several hundred million years ago with the evolution of synaptic nerve nets and central nerve ganglia. Regulation of patterned contraction of muscles for orderly behaviour, ranging from rhythmic interactions of respiratory muscles, to the control of posture of the limbs and the control of muscles of speech, involves central nervous mechanisms regulated by negative feedback. Thus the brain sends motor impulses to contract muscles; the contraction stimulates sense organs in the muscle which sends impulses over sensory fibres back to the central nervous system informing it of the degree of muscle action; the central control centre responds by modulating, increasing or inhibiting further motor output. The constancy of control of our internal environment, the control of hormone balance, heat regulation, cardiovascular control, the balanced activity of groups of cells in the central nervous system—cord, brain stem, reticular formation, cerebellum, basal ganglia, and cerebral cortex—are examples of mechanisms controlled by negative feedback. All co-ordinated behaviour, conscious and unconscious, uses these mechanisms—without them organized purposive behaviour would be impossible. The behaviour of the organism as a whole in adjusting to its external environment is controlled by information fed back to it in response to its behaviour—words are spoken and acts performed producing responses from the environment, including our fellows, and these responses act as feedback to modify one's behaviour further.

Feedback to the organism of information from its external environment determines learning and conditioning via

"rewards" and "punishments". Behavioural scientists and neurophysiologists are making advances in understanding the mechanisms involved in behaviour at many levels. Throughout all of these studies there runs the tacit hypothesis that behaviour is dependent upon physicochemical events in cells, especially those of the brain. There is no reason to abandon this hypothesis despite our present ignorance about the regulation of behaviour, including thinking.

To some students of behaviour, free will is an epiphenomenon —an illusion, since all behaviour may be regarded as a result of our phylogenetic development and of the individual's experiences. It is maintained that what a man is and all that he knows is a result of information passed on to him by the deoxyribonucleic acid (DNA) code of his genes and by the sensory information he receives throughout his lifetime. Democritus expressed this 2,300 years ago when he said, "We know nothing unerringly, but only as it changes according to the disposition of our body and the things that enter it and impinge upon it." However, the fact that we can never know in detail the meaning to an individual of his wealth of past experiences, or the details of his genetic make-up and its impact on the functioning of his brain, means that much of his behaviour must remain relatively undetermined, and man may be considered to have free will. That this may be an illusion is unimportant. Anatol Rapoport has pointed out the paradox that if a person predicts his own behaviour and then behaves in the way he predicted, he concludes he has free will. But if that person predicted another person's behaviour and that other person behaved in the way the first person predicted, then the first person would conclude that the other person did not have free will. Yet there is no operational or logical difference in the bases for the two predictions. D. M. MacKay has recently called my attention to his views on logical indeterminacy which shed, for me, refreshing new light on the ancient dilemma of freedom and determinism[2]. He points out the logical impossibility of predicting a decision to be made by someone who is first informed of the prediction of what his act will be.

In all human relations accountability is a necessity. Empirically I cannot see how a society emancipated from magic, superstition and animism can function unless individuals *believe* that they are free and responsible for their actions, and unless society can hold them responsible. Certainly our deepest convictions tell us we are free to make choices. I believe that this intuitive conviction has been important to our survival by natural selection. The brain is an organ of adaptation, adjusting behaviour by way of feedback of information from the environment, including information resulting from the organism's actions upon the environment. Freedom to choose alternative courses of action appears as a conscious concomitant of adaptation of the individual to his environment. Experiences of what we consider to be our own freedom imply the freedom of others. It thus may follow that the belief in one's freedom to choose alternative courses of conduct may be intrinsic to the cybernetic nature of brain function.

CONTROL OF BEHAVIOUR

The idea of the control of one person by another usually elicits strong adverse reactions in people. We treasure our convictions of freedom, and know either at first hand or vicariously the misery produced by coercion and tyranny. But we often fail to recognize that we are continually controlled in a variety of ways. Sanctions are derived from parents and other representatives of society, by laws and customs, and by the impact of irrational persuasion through myths and symbols that appeal to our subconscious drives, and may have little to do with the reason and logic we believe we use in making choices. A huckster or political propagandist may make us wish to have things we would be better off without. We are none the less controlled because we wish to do the things we do.

The great problem of control of behaviour resides in the question of who controls whom and for what purposes. It is clear that control by a Hitler or a Stalin is bad; but control is real and pervasive. How can it be used to advance human welfare?

We control each other in a great variety of ways. Force and the threat of force, which are clearly objectionable, may not be used but education, persuasion and moral pressure have the same effects. Cajolery, seduction, incitement and a variety of other techniques are used. B. F. Skinner has pointed out[3] that ethical counter-controls in most countries prevent exploitation by the use of force and deception. But he emphasizes that there is real danger that the rapid development of new techniques of control will outstrip counter-control. Despite objections, science will increasingly facilitate control of human behaviour and it must be used wisely if we are to avoid disaster.

The behavioural sciences have developed new methods to modify and direct conduct. Examples are Pavlovian conditioning and the conditioning methods developed by Skinner, which have become widely used in studies of animal and human behaviour. By the use of appropriate reinforcing stimuli, behaviour may be modified and directed. The techniques involve carefully programmed rewards, reinforcing the subject's known hierarchies of values. Operant conditioning is the basis of the programming of teaching machines which are increasingly being used in education. The use by advertisers and others of subliminal messages in television has caused alarm and been made illegal in some countries. The effectiveness of this clandestine form of subconscious communication is, however, questionable.

C. H. Waddington, in his book *The Ethical Animal*[4] has considered that the long range objectives of the control of behaviour are ethical systems, the values of which may be judged in relation to their ability to further a desirable evolutionary direction, unique for mankind, and he discusses the nature of this evolutionary progress. Human culture, he points out, is based on a mechanism that requires people to be brought up in such a way that they accept beliefs given them by others such as parents and other influential persons in authority. Of course such beliefs are subject to later testing and rejection or retention, but before this can happen ideas must be transmitted as a form of social heredity. Ideas thus function in cultural evolution in a way

analogous to genes in biological evolution, and Henry A. Murray has referred to germinal ideas as idenes.

The moulding of the newborn human individual into a being ready to believe what it is told seems to involve many very peculiar processes, which at present may be explained as the formation of the superego and the repression of the id, to use Freudian terminology. A frequent result of the process seems to be that people believe too much and too strongly. The process that evolution has provided us with seems often to lead to considerable exaggeration of the ability to believe.

Waddington argues that many of the world's evils and social ills stem from over-activity of the superego, leading to the acceptance of socially regressive beliefs with undesirable impact upon politics, religion and group identifications. Intense and irrational loyalties stemming from early authoritarian acceptance of communication have repeatedly led to fanaticism, bigotry and wars. One has but to recall pictures in the American press of squawking New Orleans women with children in their arms hurling imprecations at a white father taking his small daughter to a desegregated school, to see pathological ethics in action. As Brock Chisholm has pointed out, most of the ethical beliefs we hold so strongly are established by accidents of birth and what we learn, hit or miss, before we are seven years old. Emotionally charged prejudices are propagated from generation to generation by parental and adult prestige. The strongest beliefs may bear little relation to the common good. The world has continually been sundered by the hates of rival groups and these could, in the nuclear age, soon render man an extinct species.

The rate of increase of scientific information is said now to be doubling every ten years, and its technological applications are changing society in ways for which there are no precedents. The fate of man has become the prize in a gruelling race between education and disaster. Traditional methods of education and ethical transmission appear to be inadequate, and the behavioural sciences so far have not been effective in meeting major challenges of the twentieth century. Fear that the

behavioural and social sciences may be used for evil purposes has slowed their development and blocked their use for constructive purposes. We need a larger investment of talent in these fields, commensurate with their importance. As someone has said, understanding the atom is child's play compared to understanding child's play.

CONTROL OF BEHAVIOUR BY PHARMACOLOGICAL AGENTS

The example of behavioural science best known to the public is that school of psychiatry known as psychoanalysis, which is not a science at all but a kind of authoritarian mystique based upon a variety of unverifiable assumptions. Most psychiatrists are not members of the orthodox school of psychoanalysts but use some useful Freudian concepts in dealing with the psychodynamics of mentally ill patients. So far basic neurophysiology and biochemistry have contributed little to our understanding of the causes and cures of mental illness. But there is good reason to believe that progress in brain chemistry and physiology will bring insights into disorders such as schizophrenia, and ultimately make available rational chemotherapeutic procedures. However, the purely empirical uses of shock therapy and pharmacological agents, especially when used in conjunction with psychotherapy and social therapy, have in recent years returned many mental patients from hospital to effective social life. A book edited by Hoch and Zubin, *The Future of Psychiatry*, is recommended to those interested in this topic[5].

Psychopharmacology is a new empirical field that has developed rapidly over the last decade, and the use of drugs for the treatment of psychiatric disorders has furnished its major thrust. The pharmaceutical industry has produced hundreds of compounds faster than they can be tested in the clinic. These substances fall roughly into five groups. There are the stimulant drugs, such as ephedrine and its derivatives, which increase wakefulness and decrease fatigue under some conditions but also have some undesirable side effects on the central nervous system. The anti-depressant drugs include iproniazid (Marsilid)

and a number of other monoamine oxidase inhibitors, together with some anti-depressants of other chemical types. These agents may produce euphoria, increase verbal productivity, speed reaction times and otherwise act as stimulants, but their principal value is in combating severe depressions of mental patients. The tranquillizers are a third group extensively employed in the treatment of disturbed mental patients, including schizophrenics. These drugs include chlorpromazine and a variety of other phenothiazine derivatives, as well as reserpine and a few related *Rauwolfia* alkaloids. A fourth category consists of substances that act as mild tranquillizers and sedatives. One of these, meprobamate, is sold under a number of trade names of which Miltown is perhaps the best known, and another is methaminodiazepoxide (Librium). These drugs may relieve neurotic anxiety without producing the sedative effects of barbiturates and bromides.

A fifth group of psychoactive drugs produce transient psychotic states. Their primary value is for research purposes in producing model psychoses in normal persons. Some effects of some of this group have been known for a long time. In crude form, as they occur in native plants, they have been used to produce mystical states during primitive religious rites. They include mescaline, psilocybin, the powerful synthetic psychotogen LSD-25 (lysergic acid diethylamide) and other synthetic products.

All these drugs except those of the fifth group primarily affect mood. None of them acts upon the information content of the brain. The tranquillizers and psychic energizers are primarily responsible for the large increase in discharge rates of mental patients from hospitals in recent years.

The promiscuous use of the milder tranquillizers has given cause for alarm. These substances can inhibit initiative, vigour and drive, and may have deleterious side effects. They constitute the largest item of sale in American drug stores today. Barbiturate sleeping pills, bootlegged from druggists, are being used as a substitute for alcohol by some juvenile groups. A drink called a "goof ball" is made from sleeping pills dissolved

in Coca Cola, and barbiturate addiction has become a serious problem among some teen-agers.

At present there seems to be little likelihood of the deliberate use of any of the known psychoactive drugs for the control of the behaviour of normal people. Even in the hands of a dictator, it is hard to see how any of these compounds could be used effectively to manipulate the actions of a population towards directed ends. Although these drugs may relieve depression and reduce anxiety in neurotic and psychotic patients, they can only disturb normal persons and make them miserable. Ephedrine and its derivatives may briefly spur a fatigued individual to greater output of activity but the subsequent hangover can negate such transient benefit. The functions of normal healthy organs, including the brain, have not so far been improved significantly by the use of drugs. This is true of the use of drugs in athletic contests and other competitive events. Although some pharmacological agents, including alcohol, may make a person believe he is able to perform tasks more effectively, tests indicate that this is not so. For further discussion of these and related matters the reader is referred to essays by J. O. Cole and other authors in *Control of the Mind*[6].

There are historical examples of the use of drugs to control populations. Alcohol was used deliberately by some of our American forebears to debilitate and destroy the will to resist of some Indian tribes, and oriental despots have promoted the use of opium by subject populations for similar purposes. The consumption of tobacco and alcoholic beverages is promoted by commercial interests for their own profit—a control, in general, approved by the public. But people tend to resent the use of chemical agents when urged upon them for their own good. Irrational opposition to vaccination in the past and to the fluoridation of water supplies today are cases in point. Despite the magnitude of the population problem, many most in need of birth control refuse the use of oral contraceptives even in the absence of religious taboos.

It has been popularly believed that drugs have been employed extensively in brain-washing procedures in Communist-

controlled countries. However, from the evidence available, this has not been the case. According to reliable reports, coercion of persons for the purpose of extracting confessions has involved methods similar to police state practices used since the time of Napoleon. Neither scientifically directed Pavlovian conditioned reflex procedure nor pharmacology appear to have been used in any significant way in breaking the morale of political prisoners.

EMOTIONS, BEHAVIOUR AND BRAIN SURGERY

Extensive work by neurophysiologists, using operations on the brains of animals, has shown that it is possible markedly to modify emotional and aggressive behaviour. When experimental lesions in monkeys are carefully restricted to the pyriform lobe of the amygdaloid complex and hippocampus without interference with neocortical regions, most fear and anger responses disappear, without gross motor or sensory deficiencies. Although these animals can express anger and rage in response to appropriate stimuli, they are rendered remarkably docile and fearless, and their behaviour is accompanied by a reduction in sexual activity. Studies of cats, including the lynx, show there is marked docility following bilateral lesions of the pyriform lobe. But the amygdalectomized cat can be turned into a vicious and rageful animal by additional superimposed lesions in the ventro-medial nucleus of the hypothalamus. Changes have been reported in the hierarchical position of individual rhesus monkeys from dominant to submissive positions in the pecking order following amygdalectomy, and clinical observations indicate that some amygdala lesions in man are followed by diminished social aggressiveness.

It thus appears that surgical operations on the brain's limbic system can markedly change emotional behaviour. Presumably chemical agents may ultimately be found which will act selectively on specific brain centres and have similar effects. It has been reported that cats exposed to certain agents of potential use in chemical warfare are terrified at the sight of mice. Despite the values of the neurosurgical findings to medicine, it is

difficult to see any practical application of psycho-surgery in the future, to enable men deliberately to control each other's behaviour in any socially significant way.

There is however one field which may hold promise for constructive purposes. It is possible that agents may be found to facilitate learning, memory and recall. It would clearly be desirable to find chemical and pharmacological procedures to facilitate processes of education, even at the risk of their perversion for political purposes.

CHEMICAL FACTORS IN LEARNING, MEMORY AND RECALL

Experimental work of a variety of investigators, such as the classic studies of learning in the rat by Karl Lashley, together with clinical observations on man, have shown that specific memory traces are not well localized but are diffusely distributed over extensive brain areas.

Retrograde amnesia, as seen in Korsakoff's syndrome, and which may also result from head injury, cerebral anoxia, carbon monoxide poisoning and electro-shock therapy, indicates basic differences in the nature of recent and old memory traces. Advancing amnesia extends back gradually in time, obliterating memories progressively to more remote episodes, perhaps leaving only childhood experiences intact. There seems to be no relation between the importance of the memory retained and its loss. Recent memory, *per se*, is the more vulnerable, and recovery occurs in order of time with the more remote memories returning first.

Recent evidence indicates that there are two quite different processes involved in establishing memory traces. There appear to be reverberating electrical circuits in patterns of action of many neurones in the early stages of the recording of information. Electrophysiological recording shows the presence of this kind of activity but this cannot account for the permanent storage of the trace. Lorente de Nó has pointed out[7] that "Apart from the wasteful nature of such a storage mechanism the assumption of circulating impulses cannot overcome the difficulty of explaining how memory can persist after severe shock

or deep anaesthesia, i.e. after the circulation of impulses through a large number of cortical chains of neurones has stopped." He cites evidence obtained by Alexander Mauro and M. B. Rosner (unpublished) that memory persists after long-lasting total cessation of cortical activity. In hibernating animals cortical activity, electrically recorded, ceases entirely and cannot be elicited by electrical stimulation, however strong. Nevertheless, hamsters awakened from such sleep are able to perform previously learned tasks just as well after hibernation as before. Enduring memory thus appears to be based on some enduring chemical changes in the submicroscopic compartments of neurones. Lorente de Nó concludes: "Circulation of impulses must precede and be the cause of the establishment of memory, but however memory may be stored, in the evocation process circulation of impulses must again take place to reproduce the sensation caused by the original experience."

Studies of maze learning in rats indicate that there are two stages of information storage. An initial process presumably involves continuity of nerve impulses traversing circuits, and in a later process some sort of permanent consolidation of chemical traces occurs. Thus, in rats, an electric shock across the head after a learning trial impairs learning. And this is also true of hypoxia and depressant drugs. The closer the seizure or drug administration to the end of a preceding trial, the more severe is the learning loss. This is not due to punishment effects since electric shocks delivered to the legs have no such results. Electric shock across the head does not affect learning if the shock is given one hour after the learning trial. Investigators have reported that maze learning in rats was impaired when thiopental (thiopentone sodium) was administered one minute after the end of each trial but after thirty minutes no such effects were noted. McGaugh and co-workers have impressively demonstrated that stimulant drugs such as strychnine and picrotoxin administered either before or after a learning trial increase the rate at which learning proceeds. The improved learning, when injections are made before the trial, could be due to increased motivation, alertness, etc. But their finding

that injection of the stimulant drug *after* completion of the trial improves learning indicates that the drug has affected consolidation of the learning process directly. The apparent facilitation of storage of acquired information by the use of drugs, as reflected in improved learning, suggests that possibly in the future there will be interesting practical applications to the learning process.

What is it that constitutes the chemical change in neurones associated with the storage of information? Studies show that the ribonucleic acid (RNA) of neurones is markedly increased when the neurones conduct impulses and this increase is accompanied by enhanced protein synthesis. The protein so synthesized in response to activity may represent the memory trace. The structure of deoxyribonucleic acid (DNA) molecules in the nucleus of egg and sperm is the information code of the gene which informs each oncoming generation how to make a person. As a template it synthesizes RNA which then produces the cell's proteins, including its enzymes. The hypothesis that modifications of neuronal RNA may be the basis of information storage in the brain is therefore very attractive since DNA and RNA with their highly specific code of arrangements of patterns of four linked bases are already known to constitute the blueprint for heredity.

Holger Hydén and his collaborators have developed elegant microchemical methods to study individual neurones in different parts of the nervous system in relation to their content of RNA and proteins before and after they have been involved in conducting impulses. When tricyano-aminopropine, a dimer of malononitrile, is administered to rabbits (20 mg./kg.), after one hour it elevates Deiters' nerve cell protein by 27 per cent, with an accompanying increase in this cell's RNA of 26 per cent. Moreover, tricyano-aminopropine changes the relative amounts of two of the four bases that constitute by their arrangement in the RNA molecule the code of information necessary for specific protein synthesis. Of special interest in this connexion was the finding that tricyano-aminopropine administered to human subjects is followed by an increase in suggestibility. Hydén

considers that this substance or others might affect mental states in such a way that a police-controlled government, by putting such agents in drinking water, could make propaganda more palatable. Hydén has summarized some of his thinking about the establishing of permanent memory traces as follows:

"The modulated frequency [of nerve impulses] generated in a neurone by a specific stimulation is supposed to affect the RNA molecule and to induce a new sequence of nucleotide residues along the backbone of the molecule. This new distribution of components will then remain: the RNA has been specified. This leads also to a specification of the protein being formed through the mediation of this RNA.

"By a combination of this specific protein with the complementary molecule, the transmitter substance at the points of contact with the next neurone at the synapses is activated. This allows the coded information to pass on to this next neurone in the chain. The reason for the response of this next neurone is that the protein which had once been specified through a modulated frequency now responds to the same type of electrical pattern whenever it is repeated. The specific RNA and protein are constantly produced in the neurone. From a statistical point of view, the molecules can be estimated to furnish the necessary permutation possibilities to store the memory experience of a lifetime."

D. Ewen Cameron has hypothesized that memory losses in the aged may be due to loss of RNA from their brain cells. At the 1962 meeting of the Society for Biological Psychiatry, he reported marked improvement in atherosclerotic and in pre-senile patients in memory tests following intravenous injection or oral administration of large doses of RNA. Advanced senile cases showed no improvement from this procedure. Hydén has analysed human anterior horn cells for RNA in persons aged 3 to over 90. He found that the RNA increased significantly up to age 40 and remained more or less constant to age 60, after which it declined markedly. Certainly these investigations require thorough confirmation, but they have suggestive potentialities.

SUMMARY

We have considered the nature of purposive behaviour in the light of concepts of cybernetic mechanisms and of the brain as an organ of adaptation. Recent advances have made available new psychological, pharmacological and surgical procedures for the modification and control of behaviour, and we have discussed some of their applications and limitations. Human behaviour is controlled and directed by a variety of processes, many of them subconscious and irrational. It is argued that pharmacological agents and psycho-surgical techniques now known to be of value in psychiatry and for purposes of investigation are not likely to be used as agents for the deliberate control of behaviour of normal persons. Recent studies of learning and memory may, however, in the not too distant future, come to have practical applications in education or for the exploitation of the public by propagandists. The major question is, who controls whom and for what purposes? The rôle of the behavioural sciences in establishing ethical beliefs and the operations of conscience are pregnant with potential benefits and dangers for mankind.

Advances in sciences are doubling accumulated information every ten years. Nuclear weapons and the population explosion are examples of unprecedented changes which demand new ways of thinking and behaving, if we are to survive and continue cultural evolution. The behavioural and social sciences, if wisely used, can be of great assistance in meeting these and other new challenges.

Future of the Mind

BROCK CHISHOLM

MAN'S existence now, and for the first time, is threatened. The threat is produced by man's own extensive interference with the biological function of his mind. It is his mind which constitutes man's major difference from, and competitive advantage over, other forms of life. His mind has enabled man to control many aspects of his physical environment, to adjust effectively to those aspects he is not yet able to control, to compete successfully with all other forms of life on earth and completely to control most of them. In recent years man has extended his knowledge and controls into the submicroscopic world of the filterable viruses and the atom, and he is now adventuring into the vast areas of space. Increasingly he is gathering material with which his mind can work more efficiently, and is developing his mental skills. During this long process of increasing his knowledge and skills man has come into possession of enormous power, which he is using both constructively and destructively, for and against his physical environment, other forms of life and himself.

Not all man's thinking patterns have been uniformly successful. Many of them were effective only temporarily or locally under special circumstances, and whenever they were carried over into other circumstances or times disaster could result. Some ways of thinking became rigid and authoritarian and were imposed on whole populations and supported by powerful priestly and lay hierarchies. Any such rigidity, or pretence of possession of final truth, has slowed, distorted or even halted man's intellectual, scientific and social development for long periods, and over large areas. Whenever an unquestionable orthodoxy has been proclaimed, imposed and accepted,

freedom of thought has been treated as a public enemy and strongly suppressed, yet freedom of thought constitutes man's primary instrument for survival.

Fortunately man's inherent drive to use his intellectual equipment, his mind, is so great that suppression of independent thinking, no matter how ruthless, has never been complete, and heretics have always risen to challenge orthodoxies, even at risk of their lives. The human race owes most of its valuable progress to its heretics, the people who insisted on changing belief and behaviour patterns to fit tested new experience and knowledge, independently of the ancestral or authoritarian dictates.

In very recent generations, at least in many parts of the world and in the fields of knowledge allotted to the physical sciences, freedom to think independently of custom or tradition has been firmly established, but this freedom was not gained easily or quickly. Orthodoxies had extended their paralysing controls even into astronomy, physics, chemistry, anatomy, geology, and many other branches of knowledge, and had forbidden new interpretations of the experiences being gained by observation and research in such fields. It has taken many centuries to force relinquishment of the belief that revelation and faith can provide an appropriate authority in human knowledge, and the job is not yet completed. Many people continue to hold many untrue and irrational beliefs simply because they were taught them in their childhood or by a loved and respected person. For example, many hotels have no floor or room numbered 13 because too many of their patrons would not use any floor or room so numbered. Such an example may, at first glance, seem irrelevant to this discussion, but it does illustrate the kind of misuse of the function of the mind which produces most of man's major problems and now threatens his existence.

This type of misuse is the uncritical acceptance of parental, ancestral or local patterns of thinking simply because they were learned early in life and so classified as "good", which determines truth in the minds of many people. Use of such patterns

can, and commonly does, persist even when they have become dangerous and self-destructive, as in the case of warfare at the present time. It should be obvious to anyone of even below average intelligence and with little education that warfare has become mutually destructive, suicidal and no longer a sane diplomatic instrument, yet many nations are doing all they can to increase their ability to kill, in the tragic belief that such activity will increase their own security. So many of their citizens retain that outdated faith that heads of governments, even if they are themselves intelligent and well informed, are unable to change from their traditional international "posture" of threatening any real or potential enemy.

This wide-spread disability, a crippling of men's minds by uncritical acceptance of early imposed attitudes, has been regarded generally as virtuous and admirable. Under the name of loyalty it has been used to keep the younger and more independent people under the control of the "establishment", the old people, the orthodox, the hierarchies, and has prevented appropriate change when circumstances and conditions of survival have changed. It has ensured the passing on of prejudices from generation to generation, often almost intact, and often very damaging to the receiving generations.

For many centuries man has survived by groups in competition to the death with other groups. For the survivors it has been a successful method. Although the scale has grown larger, the principle has changed very little. Our remote ancestors belonged and owed loyalty only to very small groups, at early stages only to the family. This was the survival group, whose head was autonomous, held power of life and death over its members, owed no obligation of concern to anyone outside the family, and demanded absolute loyalty to his or her will, which was the dominant or even the only social morality of the era. Over a long period competition demonstrated the advantages of greater numbers of fighters and workers and the family enlarged to include several generations and collateral lines. It was able to compete more effectively and so tended to survive. Its growth continued by capture of women and slaves and its

own natural increase until it became a clan, composed perhaps of many families who would generally all be related through a common ancestry. The social conditions had changed little. The head of the clan still held absolute authority. He might be advised by the heads of families and by the current representative of the clan's god or gods, or he might himself hold that position too. Still the undivided loyalty of the members of the clan to its chief was a first moral principle and was not diluted by any concern for the welfare of anyone outside the clan.

Inter-clan warfare again showed the advantages of numbers and, by voluntary formations of alliances of clans, by marriages between ruling families and by threats or capture, clans coalesced into tribes, which in some cases attained very considerable size. Apparently the authority of the head of the tribe was still absolute but probably tribal councils gradually assumed or were given increasing importance in decisions affecting the welfare of the tribe. Power of life and death and the right to absolute loyalty were still the normal prerogatives of the chief, but perhaps increasingly shared by the shaman or priest or the tribal council. The tribal gods increased in importance through the teaching of their representatives and always the change was in the direction of greater power for those representatives. Taboo, dietary and social laws, threats of magic punishment and all available methods of mystification were used to establish and maintain control of the thinking of the people. The power of the chief and that of the priest commonly supported each other for their common benefit, though either might be eliminated by the other if he threatened to encroach too far on competing prerogatives.

With increasing power in the hands of an individual, various grandiose titles were assumed and, where supported by the priesthood in the name of the god or gods, divine right and power were claimed, and enforced by military and/or religious threat. Murder, torture and mass slaughter were normal instruments for the extension of such power and the establishment of principalities and kingdoms. There was also extensive appeal to the cupidity of individuals who could expect special

privilege and benefit from the ruling authority. Every prince and king was surrounded and supported by people who garnered some share of his power, wealth and privileges. The will of the prince or king or emperor still constituted a first moral obligation; it was the law. Loyalty to that law was enforced on pain of imprisonment, torture and death and was bounded by the welfare of the survival group still, whether it was the principality, the kingdom, or the empire.

Right up to the present time the ancient belief that: "The welfare, prosperity and power of the group into which I happened to be born is more important than the welfare, prosperity, power, or even the lives of the members of any or all other groups" has been held by most of the human race. Along with that faith is also held another: "Whenever we are frightened or feel threatened, the right, effective and virtuous thing to do is to increase our ability to kill other people". That was our normal method of ensuring the survival of our group in the past, but its success depended on the defensibility of our group or its ability to overcome the defences of competing groups. No group can any longer defend itself against death from attack from outside, nor can it effectively attack other groups without great risk of complete destruction of its own people. It is no longer possible to "win" a war.

The whole method of survival by groups in competition to the death with other groups has broken down. The survival group, for the first time in human experience, has become the human race itself. From now on we will survive as members of the human race or not at all, but we have no previous experience of this situation and no traditional concern or education for survival of the human race. The occasion for such concern had not arisen until about fifteen years ago and was not foreseen or provided for by our parents or ancestors. Now we are all threatened with extinction by our own traditional survival patterns, a position which most of us still find impossible to accept as real, because we have been taught from infancy to depend on our "conscience" values, and even to consider changes in them is commonly felt to be immoral and disloyal.

Though our present armament, nuclear, conventional, chemical and biological, is capable of killing everyone on earth, including ourselves, some three or four times over, very large numbers of people sincerely and earnestly believe that to increase our power to kill still further, to be able to kill everyone say ten times over, would, in some undefined way, increase our security. Of course this is entirely fallacious and irrational but such early-learned faiths are not dependent on evidence or rational thinking and persist against all experience and reality. The long centuries of conditioning to which we have been subjected will not quickly or easily give place to an era of rational thinking, even though our very existence depends on our ability to think soon enough and widely enough. We, as nations, are behaving as though the last fifteen years of scientific development in weaponry had not happened, simply because too many of us are emotionally incapable of seeing and accepting its evident consequences in relation to our survival, and of formulating new and unconventional alternatives to warfare.

This is the greatest biological threat, indeed the first universal threat, against the human race, and we have no tradition of concern for survival at that level. Concern for individual or group survival, which is traditional, is no longer adequate for the new conditions and, where it is exclusive, it is in fact now suicidal.

Because our ancestors did not develop any concern for the survival of the human race, no occasion having arisen until about fifteen years ago, we have no national institutions entrusted with or designed for that purpose. This is an unassigned responsibility which has become extremely important, but which is still left to private and voluntary initiative. Only the United Nations and its specialized agencies, among all public institutions, come close to this area of responsibility, but they take their instructions from national authorities whose concern is overwhelmingly for national interest and advantage. This system and situation represent an extensive malfunctioning of human minds which is very dangerous. It appears that the next step in social responsibility and organization is biologically

necessary, in the interests of human survival as a form of life. The transcendence of world values over local and national values is overdue and essential to survival. Its delay is, in the most literal sense, endangering all mankind.

Future of the Mind

DISCUSSION

Young: There is much in these papers that I find stimulating and interesting, but I suspect that one of the main characteristics of the future is likely to be the disappearance of the very subject matter of this session on the future of the mind. In spite of much that Dr. Hoagland and Dr. Chisholm said, the whole terminology has not yet escaped from the dualism of thinking of the brain and the mind as two separate entities. One of our most deep-seated superstitions is that although we no longer regard the liver as occupied by a spirit we persist in talking about the brain as if it consisted of two separate things, one called "matter" and one called "mind". I think that one of the most important advances in our thinking will come when we cease to trouble with this dualism.

Two salient points about these papers need to be discussed: firstly the question of brain function, and secondly the position of the individual in relation to the community as reflected or controlled by his brain.

On the brain function aspect I agree with much of what Dr. Hoagland said. Most of his presentation would have been generally acceptable to neurologists, but those who are not studying the brain should realize that a lot of the material about the chemistry of the brain, especially concerning learning and ribonucleic acid, is exceedingly speculative. The problem of memory is a very deep and important one. Dr. Hydén has done wonders with these cells, as Dr. Hoagland described, but I am doubtful whether he has yet said anything meaningful about the problem of memory. Dr. Hoagland spoke of the frequencies of nerve impulses modulating protein synthesis; I am doubtful, as a non-chemist, whether these frequencies,

which range up to 1,000 per second, are likely to have any influence at all on protein synthesis.

We must expect explosive changes in our understanding when we begin to understand the brain. Its machinery is complicated to an extent which is difficult to realize, since we are brought up to think about the brain in terms of rather simple reflex patterns. We imagine that the system is one in which we press a button and the model works. We escape by saying we don't know how the cortex functions and leave it at that. But as we begin to have ways of thinking about what happens in higher nervous centres it is very likely that our whole basic system of thought will be revolutionized in a manner that is perhaps not yet realized.

The particular aspect I want to stress is that the brain learns by setting up a model of the world, and it builds this model out of units with which it is probably pre-endowed by heredity. The components out of which the learning system builds this model of the world must be in the brain. This is a form of representation, and it is produced by selecting certain items from a pre-set alphabet and transmitting the information in terms of this selection from the code. If we get to know something about this alphabet, which I think is embodied to some extent in the shapes of the cells in the brain, we should begin to have an entirely new language for talking about, for example, form perception. We should understand a great deal more about how we recognize shapes, how we read, how we teach children to read, how we see ourselves, shapes, faces and people.

We at present understand only very little about this coding system. Physiological experiments in which recordings are made from single cortical cells tell us that a lot of our visual pattern is made up of oval fields assembled in the cortex by the learning process. What is this learning process? The setting up of representation out of a set of symbols involves selection. Some symbols are accepted, others rejected. I suggest that the whole system is basically concerned with limiting the number of possible things that each cell can do, by a choice between perhaps only two outputs of each cell. Each cell begins with

certain coding capacities: for example a cell in the brain will recognize vertical shapes, shall we say. It has certain outputs going to two possible pathways, such as "take" or "withdraw", to give a very simple example. What is learned is whether vertical is to be associated with "take" or "withdraw". It is possible that a cell may be switched to do one thing by inhibiting its capacity to do the other. If so, what is learnt is what *not* to do. A very simple example is the Pavlovian conditioned reflex which is so often taken as a paradigm. The sounding of the bell could make the dog salivate either more or less. We tend to think of the experiment as facilitating the pathway to salivate more. The formulation I am suggesting is that the dog is learning not to salivate less. It is switching off the "don't salivate" connexion with that particular stimulus.

If some such methods are to work, we might begin quite soon to learn something of the complexities of the whole coding system and learning system in the brain. Then we would be in a better position to learn how to teach, which is surely the thing we must talk about more than anything. To change the attitudes which Dr. Chisholm has pilloried so justifiably requires some knowledge of how to introduce alternative methods of teaching. As long as we know so little about the coding system and how it is changed we don't really know how to instruct the wise adult instructor we hope to put in the driving seat. The poverty of educational theory seems to me to be one of our great weaknesses. I think it is likely to change to an extent which may even seem frightening.

We come next to the question of the individual and his group. Dr. Hoagland referred several times to the fact that we are inevitably highly conditioned, and we must learn to accept this. We still insist on regarding ourselves, each little "gene-learning unit", as something complete and independent. Some people will still even emphasize that any "individual" could survive and live alone, say on a desert island. This is dangerous nonsense, because it obscures the fact that in practice each of us is utterly dependent on the information and the language that he receives from others. We have been endowed with these

tremendous powers by language and memory from our inheritance. I don't think, Dr. Chisholm, that it is at all likely that this will be readily abandoned. Whatever the future holds for man, it cannot hold a completely fresh start, because such a concept is really not meaningful. It is likely that the existing concept of learning will be modified and to some extent be replaced. Indeed, what is the process by which concepts become modified, particularly in the light of the history of discovery and technology? This is a really interesting problem—the repercussions between technology and biology particularly, between finding machines which imitate and supplement human weaknesses, and then the study of our own capacity by the use of the very instruments we designed in order to supplement them. This seems to me to be a very subtle cycle, which has been very little investigated and is well worth further study.

I believe the pattern of our understanding of emotion is also likely to change dramatically. Dr. Hoagland was fascinated by the monkey with the amygdala removed. It is possible to take out the amygdala today and put it back tomorrow, by cutting the brain essentially in half and occluding one eye. Then the side of the brain which is receiving the input from the open eye has, so to speak, no amygdala. The monkey is then very tame, at least in respect to visual stimuli. If you then open the other eye, which feeds the side which has an amygdala, the animal will go back to being a wild monkey. This is a very powerful technique which is going to show us a great deal about emotional responses and give us an understanding of them so that they may in future be better controlled.

The basis of a lot of the conflict that Dr. Chisholm was talking about is the question of what sort of things we react to emotionally. What are the signs that we put to each other which produce aggression, for example? Again, it is difficult for people of different genetical backgrounds to communicate. Facial communication systems don't fit, and therefore it isn't equally easy for all parts of the human race to communicate. We often tend to forget this and there might well be more studies of the difficulties which are liable to occur: such things

as that negroes have thick lips and white people have moderately thick ones and the Chinese have thinner ones. These are not the trivialities they seem, but tremendous barriers, likely to produce all sorts of failures of communication and aggression because they are part of the communication system. It is very interesting that the anthropologists' classification of races is nearly all on what they call "characters unimportant for survival". Yet these are nearly all facial characters concerned with communication! This seems another area where understanding really should improve quite rapidly and is likely to do so because people are now aware of the problems.

Incidentally, so much of what we talk about we know only from our own point of view in our own culture. I wonder if anybody knows what is the attitude, for example, of the Chinese population or intellectuals to humanity being one race? How much do we know about the development of ideas on these fundamental themes in other cultures?

Coon: The Chinese don't like that idea at all. Ever since the Communists have been in power they have been spending a lot of money sending palaeontologists around to fill the gap between *Sinanthropus* man who is about 400,000 years old and the upper cave people who are about 10,000 years old. This is so that they can prove Weidenreich's theory of the continuity of the evolution of the Mongoloids apart from the rest of mankind. Now they have got six skulls that fill that gap and they feel very happy about it.

Haldane: Dr. Hoagland said that all scientists think deterministically. I don't think that I do. I have come to the conclusion that my subjective account of my own motivation is largely mythical on almost all occasions. My mother used to ask me, "Why did you do that?", and I learned to give a list of motives. Looking back I think I was generally wrong. I don't know why I do things.

Secondly, in my opinion if a chess-playing machine is purposive, natural selection is also purposive by the same criteria.

I am in fundamental agreement with Dr. Chisholm, but I think he is a little rough with the human race when he says it

compares badly with other animal species. What other animal can walk forty kilometres, swim two kilometres and after all that climb a fifteen-metre tree? Man is a pretty good all-round beast, and that makes me a little more hopeful about the much more important issues which Dr. Chisholm raised.

I would like to remind Professor Young that in perhaps the most important of the Indian philosophies, the *samkhyā* philosophy, there is a phrase, *linga-sarvia*, which roughly corresponds to "mind". *Linga* means symbol and *sarvia* means body, so this means the symbol-body, the body consisting of models, if you like, or perhaps messages. It is something somewhere in space and time and is essentially similar to the "gross" body which is made, according to that philosophy, from a rather different kind of matter—call it electrical oscillations or whatever you please. I am inclined to think that the ancient Indian philosophies were gloriously muddled up by scribes, and very badly mistranslated, but perhaps they have something to suggest to Western philosophies.

MacKay: I agree with Dr. Hoagland that it is "necessary" to treat one another as free and accountable even though our brains be physically determinate; but I think that this freedom is a matter of fact, and not of convention, still less of "inevitable ignorance".

Suppose that tomorrow you must make up your mind between two options—say X and Y. If your brain and all that acts on it were as mechanical as clockwork, you might suppose that there must exist, in the common calculus, a formula that determines already the form of your choice, so that your sense of "freedom" is illusory.

The remarkable fact is that no such formula exists in the common calculus. Any formula such as "Tomorrow he will certainly choose X" is one that you are not merely entitled, but logically bound, to reject; for if you believed it today, your brain would not conform to the condition presupposed in the formula (namely, that you were not going to make up your mind until tomorrow). Thus whether or not an ideal "detached observer" could predict your choice, you are correct in

believing that it is undetermined by any formula in the common calculus that binds you and your observers.

This brings out a basic distinction, which I felt to be necessary in Dr. Chisholm's context, between changing people's ideas by dialogue and by manipulation. In manipulation the action is essentially one-way, and the manipulator is not precluded from depersonalizing the other by treating him as a determinate object. In dialogue, the reciprocity of the interaction makes this logically impossible, since each necessarily becomes "undetermined" (in the above sense) to the other as well as to himself.

This, I think, is the logic behind our instinct for human dignity. Man's characteristic fulfilment is in reciprocal person-to-person relationships. Any relationship in which one member is not genuinely "open" or "vulnerable"—prepared to listen—to the other, has in it a manipulative element that does violence to the essential nature of the other.

When we come to matters of conscience, we face an exactly parallel distinction, between seeking to enlighten and seeking to violate. Dr. Chisholm's talk itself offers a good example of the first. So do the efforts of most conscientious parents, however different their views may be from Dr. Chisholm's.

To force a man to violate his conscience is something quite different. It is always an evil, even if at times the lesser of two evils. This is part of what is meant by the absolute authority of conscience. To enlighten one another's conscience, on the other hand, is of the stuff of our human responsibility to one another. No sane parent can rightly be relieved of it, however many others may be allowed to share in the dialogue.

The easiest way to see the force of this is to ask how Dr. Chisholm would feel about his own right to pass on his humane view of life to his children. Surely the passion with which he speaks belies any suggestion that for him there is nothing authoritative or objective about the enlightenment he offers. We ourselves could not honestly agree that his children would be equally justified in flinging his teaching aside.

In other words, I am pleading for a realization that although conscience can be warped, moral perception is not wholly

arbitrary. There is such a thing as enlightenment—and its counterpart, moral blindness—to things which, once seen, are seen as objective. Only the expulsive power of a new perception, and not any authoritarian manipulation, can bring about a morally viable refinement of conscience.

Coon: Without people manipulating others you would have no set events, and without set events you would have no social institutions and there would be complete chaos. So it is not a question of whether people can manipulate one another or not, but of whether they can do it with the minimum of friction.

Brock: What Dr. Chisholm said in essence answers a question asked earlier by Bronowski: what is the problem that we are trying to tackle? There is no evidence that man has deteriorated; there is, however, abundant evidence that he is not moving fast enough in relation to the enormous acceleration of environmental change today.

This brings me back to prediction. According to scientific method, we have only one acceptable method of predicting, and that is to extrapolate from existing knowledge. Earlier we agreed that to progress into the future we have to have a hypothesis and put it to the test of experiment. Our real problem is that we have got to carry out experiments, the answers to which will only be evident fifty or sixty years hence, and none of us know how to carry out such experiments. For example, food is important as one of the many factors that determine our constitution. How should I feed children today to give them a sound constitution fifty or sixty years hence, when they will be attacked by atherosclerosis and cancer and degenerative diseases? How can I test any hypothesis about how to feed children today for that purpose?

Similarly, Dr. Chisholm has told us that what man needs is a new kind of conscience, a new kind of understanding, which will be different from the kind we ourselves were given in the first five years of our lives, since conscience is largely determined in the first five years of life. What we want to know today is: what do we teach children today that will give them a better conscience when they get into positions of authority fifty or

sixty years hence? What method of experimentation enables us to set up a hypothesis and to test it on the assumption that we will have our answer fifty years hence? Isn't this the problem?

Medawar: I don't believe it is. I have been wondering what is rather peculiar and unrealistic about this kind of discussion. Perhaps it is this: we *already* have that kind of control over behaviour and therefore, in a figurative sense, over the brain, which with other bodily systems, such as the endocrinological or the immunological, comes only from a deep knowledge and understanding of how they work. We don't really have to know anything about neurophysiology or neuropsychology to put Dr. Chisholm's recommendations into effect. We already have the appropriate kind of control over the mind. If we did the kind of things that John Young wants to do, we might do the job much more quickly and much more effectively; but what impedes us from putting Dr. Chisholm's recommendations into effect is that people are indifferent, or people don't agree about what is best to do. It is not lack of knowledge about how the brain works, is it?

Young: I don't agree. We even lack detailed knowledge of what the relevant signs are that elicit aggression. Worse still, we don't know anything precise about the process by which we learn to react to members of our own group; or how we learn languages or mathematics. How can education be fully effective while we are so ignorant?

Lederberg: Man has believed in education since Plato, and there is as yet no direct evidence that it in fact works in any predictable, constructive way. I don't think we really know how to educate children so that these concepts can be instilled.

Medawar: I think it is mistaken to say that we don't know how to educate children although I am sure there are better ways of educating children than those we know now. But if we confine ourselves to the kind of thing Dr. Chisholm was saying, I don't think we should say that lack of technical knowledge is any obstacle to putting them into effect.

Huxley: We want a great deal more research on how conscience itself is formed, before we can begin to modify it. It isn't formed in the school period, though it may be modified then.

Brain: We are dealing with established reactions, which are the product of consciences built up in people many years earlier. We may now modify consciences, if we start at the beginning, but how are we to modify the established reactions? Isn't that the crux of it?

Hoagland: There is a long phylogenetic history to the aggressive behaviour with which we are concerned. Konrad Lorenz has pointed out interesting things from studies of animals. As we well know, most animals fight for status in the "pecking order", and do this with vigour and enthusiasm. I suppose about the only animals that don't fight are clams and oysters, probably because they can't get at each other. Combat seems to be an essential part of the development of societies of mammals and birds and of the whole vertebrate series as well as most invertebrates. Lorenz and others have observed that when well-armed animals like wolves, lions and sharp-horned ungulates fight for status, they rarely kill each other, or even do each other much harm. Their combat is more in the form of a duel. On the other hand, Lorenz found that two turtle doves caged together pecked each other to death, a thing which hawks would not do. Doves are very poorly armed. Lorenz points out that male rabbits may fight to the death if they cannot run away from each other, whereas this never seems to happen with the well-armed animals that have surrender signals and yield status in defeat. Man is notoriously ill-armed biologically. We have no fighting canine teeth, or horns, or heavy armour. We cannot run very fast, and our skin is thin. We appear to be more like the dove or rabbit than the hawk or wolf. In 1935 Lorenz remarked that the time may come when men have developed such powers of mass destruction as to threaten the human race. He said that the great question then will be whether men will behave like wolves, or like doves. Let us hope it will be like wolves.

Young: Animals of all sorts indulge in symbolic conflict. This is a very important point which has not been nearly sufficiently realized. Professor Wynne Edwards of Aberdeen has written a very interesting book on this, *Animal Dispersion in Relation to Social Behaviour*[1]. Right through the whole animal kingdom animals engage in symbolic conflicts in order to distribute themselves appropriately around the area available.

Huxley: This is an important and exciting idea, which needs following up in the human field.

As regards the problem of conflict, the wolf story is really extraordinarily interesting. Wolves are social animals and, as Lorenz showed, if there is a fight between an older and a younger wolf, and the younger wolf is being beaten, he adopts an appeasement attitude, presenting the nape of his neck to the other, and this automatically inhibits further attack.

I was once with Pavan, the South American geneticist, in the Great Smoky Mountains, and we came across the first wild bear either of us had ever seen. We got out of our car to take a picture and Pavan for some reason made a face at the bear, whereupon the bear made the same sort of face back and rushed at him: I have never seen anybody run so fast. Pavan's grimace was an automatic sign-stimulus for the bear, calling out a completely genetic reaction. We often react in a similarly automatic way, but to learnt sign-stimuli, such as God or Fatherland.

Klein: Karli in my laboratory has been doing experiments for several years now on interspecific aggressive behaviour between rats and mice. There are rats which spontaneously and constantly kill and others which never kill a mouse, and we do not clearly see today where the individual differences are. Stereotaxic operations on definite areas of the forebrain or on the amygdala can, however, transform non-killers into killers, and killers into non-killers.

I feel that hormonal control of behaviour has been pushed into the background. Dr. Pincus did not tell us anything about hormonal control of classic sexual behaviour. Even the behaviour of a particular rat can change in a few hours. Karli has

shown that if you put a mouse with a pregnant rat for days, the rat will take no notice of this mouse; then just 24 hours before parturition takes place, the rat will suddenly treat the mouse like a newborn rat, even if the mouse kills the litter. This is hormonal control, performed through the ovary.

Pincus: I would like to question for a moment the assumption that everybody has made, including Dr. Chisholm, that what is taught in childhood very strongly influences later behaviour. Two phenomena have struck me. One is the one which Dr. Klein has remarked on. Coming to the rescue of endocrinology, I will say that one can markedly alter behaviour, particularly the "pecking order" behaviour that Dr. Hoagland spoke about, with hormones, and I don't think I need to stress that here. The other thing which has always interested me could for want of a better word be called "adolescent rebellion", in which the adolescent almost automatically rejects many of the precepts instilled by parents. I would like to hear more detail about this. How influential is it, in fact? Can it be used as a basis for reforming the human race?

Szent-Györgyi: If I understand Dr. Chisholm properly, we are in a vicious circle, because the adults teach the children. What can be done to break the circle?

Chisholm: There are certain times at which people are more amenable to new information than at other times. For instance, young married or engaged people are sometimes willing to listen to attitudes that they were not willing to listen to previously, because they may feel some timidity about the responsibility they are taking on, and they are not quite sure how to cope with it. Also, sometimes during the first pregnancy in the family, the potential parents begin to concern themselves about what their responsibilities to a child will be; some of them quite suddenly realize that there is something to learn about it, that there really is no God-given certainty about their fitness to bring up children effectively. There are possible approaches at those times that can break this vicious circle.

Szent-Györgyi: Children are very important, and the rights of a father over his children have been reduced more and more

over the years. In Roman days, the father had the right to kill his children, but today if I invite my cousin to come over to my house he says "I can't come, I have no sitter, and I would be taken to jail for leaving my children alone". On the other hand every parent has a right to fill the brain of his child with the most complete nonsense, and to engrain it so deeply into the brain that the child can never get rid of it. This is a right which should be abolished.

Huxley: Surely you wouldn't say that a parent has no right to inculcate anything into his children? Bertrand Russell started a school at Telegraph Hill, where the children were to do everything they liked; on principle, he was never going to rebuke them or punish them. He was once asked whether he had ever had to punish any of the children and he said, "Well, I did once, regretfully, when I found the older children putting pins into the younger children's milk".

Comfort: We haven't yet discussed the time-honoured problem of revolution—which, although we have not used the word, is what we are discussing—of how to bring about a fundamental change in society by planning. I agree with nearly everything Dr. Chisholm said, but didn't he a little underrate the sociality of man in his suggestion that human beings generally adhere first of all to the local group, and have very little feeling, say, for what happens in south-east Asia if they live in Europe? This is to a large extent true; it is true because it is very difficult for people who are at a great distance and out of sight to have the same empathy as those who are near. But our social behaviour is really built up originally from these group loyalties, and it is by acquiring a group loyalty within the family that we acquire a loyalty to the human race.

One of the troubles is, of course, that today we get no chance to express that sociality to the full, because nearly all the more deplorable policies are a result of our habit of delegating decisions to individuals over whom we have little control. I think the average sense of the human race would have been very much against, for instance, Hitler's activities, or the activities of bomb manufacturers. Such activities have in each case been

the work of individual psychopaths, or individual people in office to whom we have delegated decisions. From what we have heard in this meeting, though, I can't say I have very much more confidence in delegating them to egg-heads. I feel, without being personal, that any person here who found himself obliged to take the same kind of decisions would be subjected to stresses which no human personality, however intelligent, is really adequate to cope with.

I have become more and more convinced, as I listened to these very liberal and very intelligent comments, that there is an enormous survival value in human bloody-mindedness. Even if we could make a chemical substance which increases people's suggestibility, the British public might be able to resist this. In those who have once acquired the habit of contrasuggestible response to propaganda, I think that would be the response which such a drug might well enhance. This resistance on the part of the common man to being over-manipulated, either by dictators for pathological reasons, or by scientists for the most admirable ones, is the chief survival value today, which I, as a good anarchist, would like to see propagated.

Pirie: Don't different communities vary in their concentration of bloody-mindedness, to use your excellent phrase? It always seems to me that the British, especially the Scottish, are particularly well endowed with it, and it is one of our most useful attributes.

If I can judge from my rather casual observations, bloody-mindedness is much less widespread in Germany, and somewhat less widespread in the U.S.A. How can we encourage the Germans and the Americans to become much more practically bloody-minded, and distrust their governments to the extent that we do? That would be a practical method of achieving Dr. Chisholm's Utopia.

Young: Bloody-mindedness is totally absent in China, too.

Lederberg: We are saying that the world's problems are all due to the psychopathy of man, so let us try to heal him; we know that won't happen in a hurry, so that is another way of thrusting these issues out of our minds. A lot of what has been

said is putting the cart before the horse: a lot of tensions, a lot of personal aggressiveness, all the undesirable facets of conscience that we have been talking about, are not so much the cause as the consequence of our political institutions. People who have the most idealistic consciences can sometimes get themselves involved in the most unholy and sinister type of activity through the particular political institutions they belong to. If we turn things around, won't we achieve many of the things that Dr. Chisholm was talking about? Most effectively, we must repair our political institutions as best we can with the kind of limited consciences we have at our disposal. This is not a problem of science; it is one of politics at the present time.

Biological Possibilities for the Human Species in the Next Ten Thousand Years

J. B. S. HALDANE

SINCE no statement about the future can be made with certainty—which is why it is always foolish, and often wicked, to make a promise—the best I can do is to suggest some alternative possibilities. There is however one generalization which can be made with fair confidence. Important historical events usually surprise those to whom they happen. However the study of history has at least this advantage, that to those who have learned its lessons the events of their own time may bring joy, sorrow, and surprise, but not amazement, despair, or complete confidence.

My political anticipations have usually been wrong, though I backed one winner. In 1932 I stated that the educational system of the Soviet Union was being developed in such a way that it was likely to overtake other states in science, and consequently in other fields also.

My second preliminary point is that I shall not draw a sharp line between physiology and psychology. Much that is classified as psychology would in my opinion better be classified as physiology of the senses, of muscular co-ordination, and of the brain.

My third is to draw your attention as forcibly as I can to the sea lion (*Otaria californica*) and to the late Alfred Kinsey. The sea lion has a fantastic capacity for balancing objects on its nose, and appears to enjoy doing so. Whether this species ever employs this capacity in nature I do not know. Of course, very fine co-ordination of the neck muscles is clearly useful, but the actual balancing capacity must be a by-product. The great advances in evolution have often been the use of a structure

developed to serve one function for a different one, for example a gill arch for grasping food, a gill slit for hearing, a walking leg for manipulation or flight, and a vestigial wing as a gyrostat. We have to ask whether we can hope for such changes of function in man. I suggest that two important elements of human culture, namely music and religion, are comparable to the sea-lion's capacity for balancing billiard balls. Rhythmical sound has a social function in co-ordinating muscular activities. It is not clear to me that the production or perception of melody or harmony has such a function. I happen to be tone-deaf. Similarly people can get on quite well without religion, and in nominally religious communities many people do so. Religion, like music, appeals strongly to a minority only, and leads to results of great cultural value in a few of them. On the other hand, the religious and musical minorities can sometimes be intolerant of the remainder.

Kinsey and his colleagues brought to light the immense range of variation of sexual activity not only within a single culture, but a small subsection of it (such as moderately well-to-do practising protestant Americans of European descent with university education). It might have been expected that this activity, so necessary for the survival of a species, would have been standardized by evolutionary processes, at least to the extent that eating and breathing have been, apart from the further efforts of human moralists. But matrimonial fertility seems to be found both among persons whose sexual activity is restricted to once weekly or less, and those for whom Catullus' request to Ipsithilla for "*Novem continuas fututiones*" would be a counsel of moderation. We may expect to find comparable variation in other fields on the borderline of physiology and psychology, and must beware of accepting current criteria of normality.

After these prolegomena, we must consider some alternative possibilities.

(1) Man has no future.

(2) A nuclear war will do mankind grave biological damage, and civilization will also have to be rebuilt from barbarism.

(3) A nuclear war, with such damage, will lead to a highly authoritarian world state.

(4) Rational animals of the human type cannot achieve the wisdom needed to use nuclear energy unless they live for several centuries. The ageing effect of high energy events renders this impossible at present. Hence the only hope for mankind is the massacre of the vast majority of us; the few survivors, and most of their descendants, being resistant to high energy quanta and particles, and thus capable of long life, if they escape preventable diseases.

(5) A nuclear war will not occur, but some kind of world organization will gradually develop, probably after a general disarmament.

I might add that mankind could very probably be destroyed by processes still more lethal than nuclear reactions.

I do not think that the greatest danger from nuclear weapons is the outbreak of an international war of the type usually expected. Armies, in the present century at least, have, I think, been more often used in civil than international wars, though the latter have killed more people. I think it quite as likely that a group of fanatical devotees of Mary, Marx, Muhammad, or Mammon, may get hold of enough fissile material to force their own government into submission and thus precipitate an international war, as the American and French revolutions did. Were I the head of most States, I should be more frightened of the armed forces of my own country than those of others. This is one reason why disarmament is so urgent a necessity.

Personally I do not think a nuclear war would lead to the extinction of mankind. There may well be more than enough plutonium to kill us all, just as there are enough rifle bullets to kill us all several hundred times, and enough lethal genes to kill us about twice. But the last desperate surviving rocketeers of a defeated state would hardly use their weapons to massacre neutrals. The survivors all over the world would be short-lived, and for many centuries there would be an incidence of congenital disease leading to suffering and mortality comparable with that due to infectious disease until quite recently.

Translocations and deletions of genes would be fairly quickly eliminated, and there is no reason to suspect that the mutations of other types would differ qualitatively from those already produced by radioactivity and cosmic particles. There would merely be a lot more of them. Imaginative writers with a superficial knowledge of biology, such as Aldous Huxley and John Wyndham, who have written of mutations of new types, have done a considerable disservice to clear thinking.

If the main contending powers are fairly completely eliminated, and other countries violently disorganized, we shall have another dark age, with recovery in a few thousand years, and perhaps a repetition of the disaster. Meanwhile the brown and black sections of mankind will have learned enough biology to believe that the survivors of the white and yellow races are genetically contaminated. They may massacre or castrate them, or at best subject them to rigorous *apartheid* in the arctic or some other inclement region.

The third alternative, that of the tyrant world state, is equally sinister. Suppose that one of the contending groups in a nuclear war is victorious in the sense that half its population and an organized government survive, this government would inevitably attempt to conquer the rest of the world to prevent future nuclear wars, and might well succeed. A few centuries of Stalinism or technocracy might be a cheap price to pay for the unification of mankind. Such a government would perhaps take extreme precautions against the outbreak of war, revolution, or any other organized quarrels. It might be thought necessary to destroy all records of such events; and the successors of Lenin or Washington, as the case might be, would not be permitted to learn of the deeds of these great men. Most of literature, art, and religion would be scrapped. Huxley's *Brave New World* adumbrates such a society. Owing to the large number of harmful recessive genes carried by most people, eugenics, largely directed to preventing their coming together, would be an important branch of applied science.

I do not consider the fourth alternative probable. But I think that as biologists we should envisage the possibility that

Shaw, in *Back to Methuselah*, was correct as to the social value of longevity. So I mention it on the general principle that "There is some soul of goodness in things evil".

I naturally prefer to hope that the fifth alternative will be true, and shall write what follows on that assumption. I am not unduly impressed by the prophecies of famine due to over-population. Thirty years ago responsible statisticians were writing about "The twilight of parenthood", "Les berceaux vides", and so on; and I was fool enough to believe them. It now seems that fairly satisfactory oral contraceptives are available, though they are very costly. In twenty years they should be available all over the world, and the article which an eminent Glasgow professor described as "a cuirass against pleasure, a cobweb against infection" should be a museum piece. So, I hope, will the instruments of surgical abortion now widely used in Japan and France. There is no organized religious opposition to birth control in India except from the Catholic church. If this body continues its opposition it may be necessary to forbid emigration from catholic states whose population continues to expand, until these states support religious celibacy on such a scale as to check their population growth. I suspect however that it will adapt itself to chemical contraception as it has adapted itself to usury, which in Dante's mind was a sin comparable with sodomy, though slightly worse.

India could probably support twice its present population, on a much better diet than today's, with improved agricultural methods, irrigation, and flood control. However the remarkable discoveries of S. K. Roy, which could probably raise our rice yields by 20 per cent, have attracted no more notice than did those of Shull and East on maize fifty years ago. If the world population reaches ten thousand millions we shall have to make a lot of synthetic food, besides utilizing leaf proteins directly. Why not?

If we can assume that our descendants will be free from atomic war and famine, we may ask five main questions which we should try to answer separately:

(1) What performances, given suitable environments, are

within the capacities of most people being born at the present time?

(2) What performances, considered possibly desirable, are within the capacity of a small minority only?

(3) What evolutionary trends may be expected for humanity in the absence of conscious control?

(4) What evolutionary trends may be expected if evolution is consciously controlled?

(5) How far must the answers to (3) and (4) be modified for human beings living on other planets, satellites, asteroids, or artificial vehicles?

Clearly the answer to (4) depends on that to (2). It may be that our remote descendants will be immortal, sessile, or born talking perfect English. All these have been suggested. But these things, whether desirable or not, are outside the human range at present; and as I have limited myself to 10,000 years I shall not consider them. On the other hand we know that men such as Newton, Beethoven, and Gandhi are possible, and I at least hold that on the one hand, most people, however well trained, are incapable of such achievements, and, on the other, that it is desirable that the fraction of persons with such capacity should be increased.

On few subjects is more nonsense talked and written than on the first question. Some successful people believe that everyone could do as well as themselves if they tried, others that rare innate gifts are needed. On what are probably quite inadequate grounds I consider that the truth is between these extremes. I think that one of the most important tasks before mankind is a complete revision of educational methods, whether we are dealing with learning long multiplication or rope climbing. Different children differ in the times at which capacities mature, and almost as surely in the best methods for developing them. Teaching methods appear usually to aim at developing children of a capacity a little below the median, and very great harm is done by wrong timing and wrong methods. We may have to wait for human clonal reproduction before scientific method can be applied here.

Meanwhile we can say that it has already been possible to produce an environment in which most people can go through life without any serious infectious disease except some virus diseases such as common colds which we cannot yet control, and others such as measles which we do not trouble to control. By the end of the century infectious diseases and deficiency diseases should be rare, even if there is a critical period, beginning perhaps about 1980, when healthy states put pressure on the remainder to conform. I shall not, I expect, be there to give my advice as to whether a few lice should be preserved alive, along with much less dangerous animals such as lions and cobras. I would vote against keeping even one *Plasmodium*. About the same time we may hope for methods of preventing many or most forms of malignant and cardiovascular diseases. These may involve considerable coercion, for example the prohibition of tobacco and certain foodstuffs, and compulsory exercise for adults.

It may well be that it will prove practicable to render human beings completely aseptic, the useful functions of their intestinal flora being taken over by vitamin dosage. The stimulus to such an achievement may be the desire to colonize Mars or some other skyey body without introducing terrestrial bacteria and viruses. It may, of course, well be that aseptic people will lack defences against sporadic infections, or suffer some other severe handicap. They might equally well avoid cancer and some aspects of senility, as Metchnikoff taught. To an aseptic person, producing, among other things, inodorous faeces, the rest of humanity will appear as "stinkers", and there will be grave emotional tensions, including a sexual barrier. This will at least be a change from quarrels based on religion, race, political affiliation, and economic status. If asepsis is either generally advantageous, or permits the development of certain faculties, it will, I hope, prevail.

The next stage in the struggle for health will be against congenital diseases and those of middle and late life. I do not doubt that these are largely congenital in the sense that a baby of one genotype is likely to die of cerebral haemorrhage due to

renal failure at the age of seventy, another of chronic bronchitis at the same age, while a third, of still another genotype, survives both of them but is crippled by arthritis. Perhaps fortunately we cannot yet predict which organs of a child will break down in old age.

One possible consequence of a rational geriatry may be as follows. A congenitally weak organ may fail through chronic environmental stress. One reason why I have gone to India is to avoid chronic "rheumatic" joint pains. I do not mind the heat, since I dress almost rationally, wearing as few clothes as decency permits. Infections such as amoebic dysentery, which are still hard to avoid, are no more trying than English respiratory infections. But I suspect many aged Indians would be happier in the bracing climates of Europe and Siberia. Perhaps retirement may come to mean retirement to a congenial climate, as it already does to some extent in the United States.

Far more important is to discover the capacities of young people, and guide them into suitable occupations. This is often thought to be the prerogative of psychologists. I suspect that the variations of human physiological make-up have been neglected, partly because we cannot even give them names. I am fully convinced that the recipe for happiness is doing a job which is difficult, but just not too difficult. I have suffered from the pangs of despised love, ischio-rectal abscess, the insolence of office, which is the worst of the three, and other ills. Provided I could work they were quite tolerable. Koheleth (*Ecclesiastes*) gives the formulation best known in this culture: "Whatsoever thy hand findeth to do, do it with thy might", though before him Sri Krishna had said it more poetically in India, and Aristotle more accurately in Greece. Whatever their other defects, societies such as that of the Soviet Union where men and women are regarded primarily as producers are likely to give greater opportunities for happiness than those in which they are primarily regarded as consumers, and vast effort is devoted to increasing their demands for various commodities. The success or failure of a work-oriented society may however depend on the choice of men for the jobs and jobs for the men.

The recognition of human physiological diversity may have enormous consequences. As soon as its genetical basis is understood large-scale negative eugenics will become possible. There may be no need to forbid marriage; few people will wish to marry a spouse with whom they share a recessive gene for microcephaly, congenital deafness, or cystic disease of the pancreas, so that a quarter of their children are expected to develop this condition. I cannot predict the later steps which will make positive eugenics possible, since we know the genetic basis of few desirable characters. I make some suggestions later.

The second question, as to rare capacities, is more interesting if perhaps less important. I shall begin by giving an example of one. My late father was an examiner for certificates for would-be colliery managers. Among other things they had to detect and estimate small amounts of methane. When the wick of an oil safety lamp is turned down leaving a blue flame, the methane can be seen burning above it as a faint "cap", and its concentration, within a range below the explosive, can be estimated from the size of this cap. Most people can only see the cap in darkness after a few minutes' adaptation. One day a candidate appeared who could do the estimation correctly by daylight. This capacity is certainly rare, but no one knows whether its frequency is one per thousand or one per million. It may have some drawbacks such as defective colour vision or a high demand for vitamin A. It is probably at least in part genetically determined.

Supernormal vision of any kind is certainly rare. Supernormal hearing is less so, but is only just beginning to be investigated. Supernormal smelling may be quite common. Supernormal muscular skill is highly prized when it is applied to certain sports, but no serious attempt has yet been made to measure it, or to determine how far it is genetically determined. Aptitude tests may eliminate the worst half or even three-quarters, but they do not pick out the one person per *lakh* (10^5) who might become a really superb dentist or lens maker.

One reason for this is that our consciousness is not closely connected with manual skill or muscular sense. Some would

prefer to say that our language mechanisms are not closely geared to those concerned with muscular guidance and proprioception. Nevertheless there are great individual differences. Some people say they have no kinaesthetic memory. I have. I can remember, that is to say imagine, what it feels like to ride a bicycle, to swim in various styles, to carry out several kinds of chemical analysis, and so on, and this although I am a clumsy person with little muscular skill. We have no evidence as to whether this depends on an inborn difference between myself and those who say they have no such memory or imagination.

The afferent nerve supply from organs other than skin, special sense organs, muscles, and joints, is not very rich, but it exists. So far from attending to its data, we seem to spend our infancy in learning not to do so unless they rise to a threshold described as painful. This may be the only way to avoid frequent defaecation, unacceptable sexual activity, and so on. Physiologists, by attention during experiments on themselves, can bring some of this information to consciousness. So do some neurotics and psychotics. I claim that I used to be able to detect the opening of my pylorus, and the passage of waste materials along my sigmoid flexure; between them localization was poor, but there was a good deal of sensation. A biologically uneducated person suddenly feeling what I felt might have reported that his or her belly was full of snakes, or contained a radio set controlled by communists or jesuits. For me at least sexual pleasure is much more like these visceral sensations than it is like the special senses or those of the skin or muscles.

Where do we go from here? I want to suggest three possibilities. The most obvious is the verbalization of kinaesthesia. For a million years or so our ancestors had manual skill; but there is no evidence that they used symbols. Sculpture and painting appeared suddenly in the upper palaeolithic, perhaps under 40,000 years ago, and Pumphrey and I have suggested that descriptive language started at about the same time. Writing began less than 6,000 years ago, and algebra less than 2,000.

I believe that much of our unhappiness, frustration, and conflict, arises from the divorce between muscular skill and symbolic expression. Once a craftsman can explain in words or other symbols how he uses his hands, a singer how she uses her larynx, a new era in physiology will open. Future cultures will, I believe, respect craftsmanship more than we do, and almost everyone will devote some time to it. It is striking how much more we know about our sense organs than our muscles. There may be common defects of muscular co-ordination as clear-cut as myopia, and as easily corrected.

Such heightened consciousness may be developed in many ways. Yehudi Menuhin, besides a capacity for sound analysis which may be no better than that of some musical critics, possesses a very high bimanual skill, that is to say capacity for co-ordinating the movements of his two hands. This may be commoner than is thought. Here is a way in which it might be employed.

Two-dimensional graphs have given us enormous insight into functions of a real variable. I can hardly think of a sine, a logarithm, or a Bessel function without thinking of its graph. Once one has seen a few graphs, Rolle's theorem, that an algebraic polynomial has at least one turning point between each pair of zeros, is intuitively obvious, and many more sophisticated theorems are at least plausible. But for similar intuition about a complex variable one would need a four-dimensional graph.

Supposing however that we train a child known by still non-existent tests to have the capacity for bimanual skill, to trace out lines on the (x, y) plane with his or her left hand, and simultaneously the corresponding curves in the (u, v) plane with his right hand, where $u + iv = f(x + iy)$, f being some simple function, what may we expect? To take an example, if $u + iv = exp(x + iy)$, then horizontal straight lines $x = a$ in the (x, y) plane correspond to circles $u^2 + v^2 = e^{2a}$ centred at the origin in the (a, v) plane. Vertical lines $y = b$ in the (x, y) plane correspond to straight lines $v = u \tan b$ through the origin in the (u, v) plane. Would a child trained to trace out such sets of lines simultaneously be able to transform other simple curves? Would

it realize that a sudden turn through any angle in one of these planes was represented by a turn through the same angle in the other (or in mathematical language, that mapping was conformal)? If so it would have the same sorts of intuition about functions of a complex variable as anyone who looks at their graphs has about those of a real variable. The truth or possibly the falsehood of Riemann's hypothesis about the Zeta function, which is the missing key to prime number theory, might be intuitively obvious, even if its formal proof were still difficult.

And man would effectively have broken through into the fourth dimension. As the least unintelligible account of the fundamental properties of ordinary matter is in terms of functions of complex variables, and three-dimensional intuition is a poor guide to these properties on the subatomic scale, such a break-through would be of great practical value. If, say, it were found that one person in a thousand possessed this capacity, they would have, like chess players and musicians, to develop their own vocabulary. This would probably revolutionize not only physical but biological theory.

However, a more generalized conscious apprehension and control of our bodies would be of still greater importance. If one observes a yogi, one finds that he has developed the same kind of power over his trunk muscles as a skilled craftsman or sportsman has over his limb muscles. Thus he can contract his right and left rectus abdominis independently, as a pianist can move his fingers independently. This control extends to a less extent to the heart and smooth muscles. Thus yogis can slow their hearts down, though it is doubtful whether they can stop them. They describe qualitatively new bodily sensations, such as that of *kundalini*. Their verbal accounts of these activities often appear to be nonsense; but no form of words which leads to concerted human activity is nonsense. It may be a pity that musicians use the word *coloratura* and algebraists the word "spur" with esoteric meanings. The yogis are perhaps a bit worse, but not much. In particular, I suspect that they have been grossly mistranslated. The human nervous system is said

to include six *chakra's*. This word, which is cognate with *cycle* and *circle*, is commonly translated as "lotus", and numbers of "petals" are given. It seems to me quite possible that intense introspection revealed various cyclical processes, including the alpha rhythm, and that the texts were misunderstood by later readers. The word *chakra* was frequently used for cyclical processes, such as those said to cause rebirth. Naturally enough they were represented by wheels. Other mystics report sensations located in their own bodies. Many Indian mystics say that the perception of God includes a feeling like sexual pleasure felt throughout the body. St. Teresa described the sensation as pain, but welcomed it.

I suggest that these people are in touch with reality, though not perhaps the reality which they think, as the alchemists undoubtedly were, and that the future of human biology includes a voluntary control over various bodily functions and a consciousness of them which will be related to yoga much as chemistry is related to alchemy. Yogis claim to be healthier than other people, and I think they are probably correct in their claims. I have little doubt that the autophysiologists of the future will be unusually healthy. We are quite ignorant of the extent of human congenital variation in respect of the capacity either for obtaining information about events inside our bodies, or of controlling unstriped muscles and glands. I suggest that one of the urgent tasks before physiologists is the investigation of these obscure sensations by implanted electrodes, supersonic focusing, and similar methods. I think such artificial stimulation, which would inevitably arouse emotions among other things, could be of great social value. Literature is socially valuable largely because it enables us to share the emotions of murderers like Orestes and Macbeth, suicides like Romeo and Juliet, tyrants like Xerxes and Tamerlane. Hence we are better able to control such emotions when we encounter them in ourselves, and to take avoiding reaction when we meet them in others.

The third question, as to present evolutionary trends, is very hard to answer. When we know how a character is determined

genetically we do not know what selective forces are acting on it. For example the selective value of ABO blood group membership begins long before birth, and continues into middle life, where it is manifested by different frequencies of gastric and duodenal ulcers and other diseases. It is reasonably sure that the forces of selection acting on human beings have changed drastically in one or two generations, and will go on doing so. For the last ten thousand years or so, in fact since man ceased to be a rare animal, I think selection has been mainly for immunity for infectious diseases. No doubt this has kept the level of non-specific defences, such as the capacity for making gamma globulins, from deteriorating, but most of it has been futile or harmful. Various abnormal conditions, including several abnormal haemoglobins, thalassaemia, and glucose phosphate dehydrogenase deficiency, confer resistance to malaria at the price of ill-health or even death. The hundreds of millions of deaths by which the European stocks secured resistance to tuberculosis were not merely futile, for tuberculosis is now a rare and curable disease. They were almost certainly harmful. As Penrose[1] first pointed out, selection for resistance to specific diseases is probably selection for genes which were initially rare because they lowered fitness in the absence of the disease in question. With the abolition of the infectious diseases our descendants will gradually regain fitness.

However, insofar as medical science enables people with congenital abnormalities who would formerly have died young to reproduce themselves, it is dysgenic, as has often been pointed out. The remedy for this is education. Once a man with rectal polyposis and a woman heterozygous for haemophilia realize that it would be wrong to have children, there is good reason why they should marry, using contraceptives, or after one or both have been sterilized.

We do not know how selection is acting in economically advanced countries. Most people marry, and the main selective agency is now fertility, not survival. We have little idea how much of the variance in fertility is genetically determined.

Parents of large families have a somewhat lower mean intelligence rating than the general population. But intelligence quotients or other similar measures are only partly determined genetically. It may be that the genetical factors making for intelligence do not lower fertility, while the social ones do so. I think it probable that the level of innate factors making for intelligence is slowly declining; but this is far from certain. As Penrose has suggested[1], genetical homoeostasis based on the higher fertility of heterozygotes may make it very difficult for selection to alter this mean level. What is more, we may expect changes in the direction of this selection in the near future[2].

The fourth question is almost equally hard to answer. As I have already said, we may expect a drastic reduction in the frequency of undesired abnormalities with simple genetical determination by the end of this century. But we have little notion of how to produce more superior people. Our descendants could of course use men judged superior as stud bulls. However, even if women were agreeable, many men would require a good deal of conditioning before they acted as such, or even as sperm donors. Voluntary Amphitryons would perhaps be rarer than Brewer and Muller have thought. The employment of a surrogate was apparently normal in ancient India. Pandu's biological father was a mortal chosen for holiness and appointed because the legal father was not functional. Nor was Pandu himself. His five sons, the heroes of our great epic, the Mahabharata, were begotten on his wives by immortals. His junior wife Madri had the intelligence to invoke the Asvini (twin deities corresponding to Castor and Pollux) and produced twins herself.

My friend G. C. Dash informs me that until recently the Jats, in northern India, along with ordinary fraternal polyandry, practiced eugenics as follows. A young man judged of outstanding merit for physique, courage, and other good qualities, was allowed access to all married women of a village. He was given a pair of gilded shoes which he left outside the door when performing his eugenic duties, to warn off any ordinary husband. After fifteen years or so, when his daughters became

nubile, he was killed to avoid inbreeding. But he might, and often did, leave the village with a chosen partner. Having fought in the same brigade as the 6th Jats, I can testify to their courage and efficiency as soldiers. In view of such traditions, the choice of a father other than a woman's legal husband may arouse less opposition in some parts of India than in other countries, whether artificial insemination or the normal process is employed.

Perhaps India may return to this practice. It is in fact permitted under existing Hindu law. There is, however, another possibility which I at least take seriously. We have known how to grow mammalian cells in culture for over fifty years. Human cells, not only from embryos, children, and cancers, but from a sixty-year-old man, have been grown for years on end. We do not know how to induce them to organize themselves. But we may find out at any moment, as we have already found out in the case of some plant cells. It is extremely hopeful that some human cell lines can be grown on a medium of precisely known chemical composition. Perhaps the first step will be the production of a clone from a single fertilized egg, as in *Brave New World*. But this would be of little social value. The production of a clone from cells of persons of attested ability would be a very different matter, and might raise the possibilities of human achievement dramatically. For exceptional people commonly have unhappy childhoods, as their parents, teachers, and contemporaries try to force them to conform to ordinary standards. Many are permanently deformed by the traumatic experiences of their childhoods. Probably a great mathematician, poet, or painter could most usefully spend his life from 55 years on in educating his or her own clonal offspring so that they avoided at least some of the frustrations of their original.

On the general principle that men will make all possible mistakes before choosing the right path, we shall no doubt clone the wrong people. However everyone selected for this purpose will presumably exceed the median considerably in some respect, if only as a humbug. And the greatest humbugs, like Hitler, would hardly relish the thought of producing a dozen

possible successors with their own abilities, and youth to boot. Possibly a movie star at the age of forty might have similar feelings.

Assuming that cloning is possible, I expect that most clones would be made from people aged at least fifty, except for athletes and dancers, who would be cloned younger. They would be made from people who were held to have excelled in a socially acceptable accomplishment. Sometimes this would be found to be due to accident. The clonal progeny of Arthur Rimbaud, if given favourable conditions, might have shown no propensity for poetry, and become second-rate empire builders. Presumably such a clone would not be further grown. Other clones would be the asexual progeny of people with very rare capacities, whose value was problematic, for example permanent dark adaptation, lack of the pain sense, and special capacities for visceral perception and control. Centenarians, if reasonably healthy, would generally be cloned, if this is possible; not that longevity is necessarily desirable, but that data on its desirability are needed. Centenarians who could continue to learn systematically up to the age of thirty would almost certainly be useful, and probably happy members of society.

There are several other possibilities of altering human genetical make-up besides selection. One is the deliberate provocation of mutations, probably by chemical agents, which seem more specific than X-rays and the like. This will first be attempted in tissue cultures. And if tissue culture becomes a frequent stage in the human life cycle, it may be practicable to do it on a large scale. It may also be possible to synthesize new genes and introduce them into human chromosomes. It will be still easier to duplicate existing genes, thus in some cases perpetuating the advantage of heterozygosity. There is still another possibility. No doubt, in our evolutionary past, we lost capacities which we should value, for example olfactory capacities, and the capacity for healing with little scarring which is associated with a loose skin. Hybridization with animals possessing these capacities is probably impossible, certainly undesirable by present human standards. But Muller and Pontecorvo were

able to introduce small fragments of the genome of one species of fly into another with which it gives sterile hybrids, and the same has since been done with bacteria. Such intranuclear grafting might enable our descendants to incorporate many valuable capacities of other species without losing those which are specifically human. Perhaps even 10,000 years hence this will be a wild project, but techniques progress very rapidly.

The fifth question is highly speculative, but it is time that systematic speculation started on it. The most obvious abnormalities in extra-terrestrial environments are differences in gravitation, temperature, air pressure, air composition, and radiation (including high speed material particles). Clearly a gibbon is better preadapted than a man for life in a low gravitational field, such as that of a space ship, an asteroid, or perhaps even the moon. A platyrhine with a prehensile tail is even more so. Gene grafting may make it possible to incorporate such features into the human stocks. The human legs and much of the pelvis are not wanted. Men who had lost their legs by accident or mutation would be specially qualified as astronauts. If a drug is discovered with an action like that of thalidomide, but on the leg rudiments only, not the arms, it may be useful to prepare the crew of the first spaceship to the *Alpha Centauri* system, thus reducing not only their weight, but their food and oxygen requirements. A regressive mutation to the condition of our ancestors in the mid-pliocene, with prehensile feet, no appreciable heels, and an ape-like pelvis, would be still better. There is no immediate prospect of men encountering high gravitational fields, as they will when they reach the solid or liquid surface of Jupiter. Presumably they should be short-legged or quadrupedal. I would back an achondroplasic against a normal man on Jupiter.

Human capacities for temperature adaptation are rather limited, and the invention of clothing renders them unimportant. When allowance is made for water vapour and carbon dioxide, a supply of pure oxygen at a fifth of an atmosphere would not suffice most humans. At air pressures below about a quarter of an atmosphere a pressure suit is needed. I may remark that my

late father made and tested the first pressure suit. However an Andean or Tibetan might be able to live at an external pressure of a fifth of an atmosphere. If this is the approximate pressure on Mars, as some astrophysicists believe, it may be desirable to pick colonists with Andean or Tibetan ancestry; for a suit which allows breathing at a pressure a few millimetres above that outside is both safer and more comfortable than if the difference is greater. I see no prospect, in the next ten thousand years, of adapting human beings to breathe air in which the partial pressure of oxygen is less than 1 per cent of a terrestrial atmosphere. On the other hand given an artificial breathing mixture, men can live quite happily, though for how long we do not yet know, at all pressures from $\frac{1}{4}$ atmosphere to 20 atmospheres, and very likely at higher ones.

The least understood danger is that from radiation and high speed particles. The ultraviolet and X-radiation from the sun could doubtless be kept out. But if Titov had got up into the streams of charged particles predicted by Bjerknes and more accurately by Chapman, detected more or less simultaneously by Soviet and American satellites, and now called the van Allen belts, or had run into a storm of particles ejected from the sun, he might have been seriously injured, or even killed. It may be known what thickness of heavy metal is needed to afford protection against these particles. If so, it is a secret. Almost certainly resistance to radiation is a desirable character in astronauts. It may or may not be attainable. It is a heritable character, though rare, in some bacteria. If there is a nuclear war, the survivors will have been heavily selected for radiation resistance, if such selection is possible. If so they will be suited for astronautics. Even if the danger is exaggerated it may be worth selecting resistant types when we know how to do so.

Possibly other dangers will prove even more serious. It is reasonably sure, on the one hand that natural selection in space will hardly change a section of humanity very greatly in ten thousand years, and that on the other, new human characters will be sought for and perhaps bred for, or, as I have suggested in the case of asepsis, imposed artificially.

What, then, can we hope for, ten thousand years hence, if things go as well as I can imagine them going? Do not take what follows as a probability, but as a fairly optimistic suggestion of possibilities. When I write "will" I mean, "may, with what—to my ignorance—seems reasonable luck".

Man will still be polytypic, but less so than now. He will be much more polymorphic, though I hope that the lowest 50 per cent of present mankind for any achievement will be represented by only 5 per cent in our descendants. I do not think there will be universal racial fusion. For most countries will fairly soon fill up, and will welcome tourists, but hardly immigrants. I do not believe in racial equality, though of course there is plenty of overlap; but I have no idea who surpasses whom in what. To take a simple example, a few communities, for example of Nilotic negroes, have remained at the stage of primitive communism, with no government. One such tribe includes a group of men whose whole function is to stop quarrels, not to administer justice. Perhaps these people behaved, on the whole, so decently that no government was needed. If so they may be better qualified to rule the British than the British were to rule them. When opportunities are nearly equalized, some races are found to produce far more superior people at some particular function than others. Thus in the United States people of both sexes with tropical African ancestry excel in sprinting. The opportunities for intellectual pursuits have not, of course, ever been equalized anywhere. The only tropical African who has yet made a major scientific discovery is Pascal Lissouba, who has discovered a new genetical phenomenon. My guess is that tropical Africans include more potential biologists than potential physicists. However, I think the intellectual élite of the world will be of very mixed racial origins, perhaps with a median colour about that of northern Indians today. This is because in science at any rate racial origins and ancestral traditions impose no appreciable barrier. I get on far better with intelligent Indians or Japanese than with Europeans whose interests differ from my own.

The élite, by which I mean roughly persons like ourselves who are thought sufficiently interesting to be invited from great distances, will be more polymorphic than the general population, partly because they will largely be products of assortative mating. A musician will tend to marry a musician, and so on, but such of their children as are not musically gifted will not remain in the musical caste, as they do in Indian castes. The élite will perhaps include anatomical freaks, say people with cerebral hernia whose thinking can be watched with the remote descendant of the microscope, astronauts with prehensile feet unsuited for walking, and so on. But the physiological polymorphisms will be far more important. There may be a few people on the planet who can give as good an account of the messages reaching their brains from the carotid sinus as I can now give of my auditory sensations, and better than I can give of my labyrinthine sensations. I think there will be more psychological polymorphism, and much more tolerance. Provided they do not harm others who do not want to be harmed, posterity will be allowed to try all sorts of things, including drug addiction and various types of sexual experience, which we condemn, perhaps rightly, in the present state of our civilization.

Once poverty is a state which no one has experienced, but merely an evil smell from the past, like cannibalism, I think there will be much less interest in acquiring material objects, and more and more interest in our own bodies and minds, and those of others in whom we are interested and whom perhaps we love. So far introspection has been rather barren except in so far as some mystics have had important historical effects, as often causing wars and other organized cruelties like Muhammad and St. Dominic, as making for increased love and tolerance, like Patanjali and George Fox.

What an objective investigation of the inner life, or as I should prefer to say, the study of life from inside, will reveal, is quite uncertain. It is at least imaginable that, apart from private worlds, described for example by Blake in his prophetic books and by Freud, it will reveal one or more objective realities, the same for all men and perhaps for many or all animals. I am

thinking of what some Indian philosophers call *nirguna*, That which has no qualities, in full agreement with Maimonides' and St. Thomas Aquinas' account of God (at least in the earlier chapters of the *Summa Theologica*) and in flat contradiction of the accounts given by most religious teachers. This exploration will be dangerous. Let us suppose that it becomes possible to induce proliferation of the *formatio reticularis*. If this is possible in an adult it will first be tried by a trained psychologist who volunteers for the job. Perhaps the first two volunteers will report a great extension of consciousness, while the third will go mad or develop an inoperable brain tumour. Or perhaps it may be impossible to induce proliferation in adults, and it will be necessary to do it in babies. To us this may seem horrible. I have often risked other peoples' lives in physiological experiments; and though none died, at least one was permanently injured. But they were all volunteers, and I was taking the same risks as they. The exploration of the interior of the human brain will be as dangerous as that of the antarctic continent or the depths of the oceans, and far more rewarding. The "officer in command" must be a man of proved personal courage, but not so soft hearted as to leave his post of command because his orders have led to some deaths, mutilations, or psychoses. To judge from the eagerness with which parents nowadays urge their children to risk their life in wars, and say that they have "given" their son if he does not return, I suspect that in a society with different ideals to our own, many parents would be prepared to risk their baby's life in the hope that it might develop supernormal powers.

A parallel development will be many-dimensional art, expressed by the simultaneous movements of different muscles. Of course we have already the rudiments of this art in the dance, especially as practised in India. But in its fully developed form it would imply a real or imagined following by the audience of the dancer's movements. Such art would also be expressible by symbols like the musical score of an orchestral composition; and just as, in order fully to appreciate one of Shakespeare's plays, we must see it performed, read it silently, and recite at

least some of the leading passages, so many-dimensional art will make analogous demands. It is possible that this art would reveal a set of objective truths, as the arts of counting and drawing revealed the truths which we call arithmetic and geometry.

One of the senses which seems to be much better developed in some other animals, notably migrating birds, than in ourselves, is that of time. We rely so much on the sun, and now on our watches, that we have largely lost this sense, and those who perhaps possessed it in an abnormal degree, like Bergson and Proust, seem to me to have written a good deal of nonsense. The negative aspect of time, of which death is the most striking feature, might cease to oppress us if we could realize human life as a finite pattern in time, capable of all degrees of perfection. No doubt the drugs which alter our perception of time would help in this research, though I must confess that I find *Cannabis* preparations very disappointing, perhaps because I cannot express my experience in words or other symbols.

I think that even as soon as ten thousand years in the future there will be a real prospect of our species dividing into two or more branches, either through specialization for life on different stars or for the development of different human capacities. To me this seems a terrible danger, as such species could fail to understand one another even worse than I fail to understand a human being in the stage of savagery, an orchestral conductor, or an abstract painter. And such misunderstanding can generate quarrels and even war. But this may be a short-sighted view. Our descendants will be in a better position than we to weigh the advantages and drawbacks of speciation.

It may take a thousand years or so before we have a knowledge of human genetics even as full as our present very incomplete knowledge of organic chemistry. Till then we can hardly hope to do much for our evolution. However as our fastest aeroplanes can move about 300 times as fast as a human walker, we may hope that our descendants 10,000 years hence may have evolved as much as our ancestors did in three million years. I think that the fact of genetic homoeostasis will reduce this figure to about half a million, which, however, is thought to

be about the time needed for the appearance of a new mammalian species. Even so our descendants would look pretty queer chaps to us, and behave even more queerly. Their activities will be particularly hard to classify. The same activity of a group in contemporary cultures may have analogies with ballet, religion, sport, experimental physiology, mathematics, and even magic. Some of this syncretism would be more easily understood in India than in Europe or America today; and perhaps if most of the bricks of the unified science of the future are of European origin, India and China will have provided the mortar which holds them together into a coherent system.

My prediction that our descendants will be more interested in their own biology than we are, and have far more knowledge and control of it, will be criticized. If more visceral sensations will prolong our lives, some will ask, why has not natural selection favoured their increase? As long as the main causes of early death were famine and violence, survival was best secured by attending to the external world. With agriculture and urbanization, infection became an important killer. But again the danger was from outside. Further, without a fair knowledge of anatomy and physiology introspection is rather dangerous unless, as in yoga, it is elaborately controlled. Such introspection can have very satisfactory by-products. Thus it is possible to cease to find moderate pain unpleasant. On two occasions I have walked about for a week or more with a fractured malleolus and a fractured metatarsus, which were not diagnosed because I kept on walking. I suspect that pain is a word which we apply to all sorts of sensations which we cannot adequately classify. If they become interesting they may cease to be unpleasant. Having undergone really intense thirst experimentally, I feel thirst far less than most Indians in hot weather. I have good evidence that others can achieve this state in the same way, as of course they can through religious or magical practices. It will be vastly easier when we achieve a nomenclature for our bodily sensations, which we shall only do by provoking them under carefully controlled conditions. Similarly by understanding and intellectualizing their sensual

pleasures, our successors will, I hope, convert them into servants rather than masters. One of the human goals is emotional homoeostasis. I do not think this will be achieved by the massacre of emotions, as religious ascetics have attempted, but by their integration, as our nervous system integrates the activities of antagonistic muscles.

If the capacity for consciousness and control of physiological processes is prized by posterity, steps will probably be taken to make it commoner, and it may be that ten thousand years hence our descendants will differ from us not only in achievements but in capacities and aspirations, to so great an extent that it is useless to attempt to follow them further. It is doubtless more probable that human interests may be concentrated on some different goal, such as music, economic activity, or religion. I have sketched my own utopia, or as some readers may think, my own private hell. My excuse must be that the description of utopias has influenced the course of history.

Ethical Considerations

DISCUSSION

Medawar: In some sense, the last paragraph of Haldane's paper confounds the rest of it. One of the lessons of history is that almost everything one can imagine possible will in fact be done, if it is thought desirable; what we cannot predict is what people are going to think desirable. In his predictions Haldane indulges in a two-fold exercise: saying what he thinks is possible, and at the same time saying what he thinks is desirable. By what conceivable process can we predict what people are going to think desirable even in fifty years time?

Haldane: We can't guess what will happen; St. Thomas More would have been very surprised to find Mr. Kruschev putting some of his ideas into practice.

Lederberg: For the benefit of any writer who is going to take up these ideas (although I don't think he will express them more elegantly than you did, Professor Haldane) I would like to point out a blind spot in most of our utopian thinking about the modification of man. We seem to prefer to put off the problem by talking in terms of the next ten thousand years, which is the kind of time-scale on which genetic modification could just begin to be plausible. On a very much shorter time-scale, we are going to modify man experimentally through physiological and embryological alterations, and by the substitution of machines for his parts. I wonder to what extent it is really worth thinking about genetic modification until we have made full use of these other methods. If we want a man without legs, we don't have to breed him, we can chop them off; if we want a man with a tail, we will find a way of grafting it on to him.

Young: In the communication sphere especially, the development of prostheses of all sorts, from computers onwards, produces possibilities which are quite fantastic. We cannot imagine what sort of answers we may be able to get to problems which now seem utterly insoluble, just as this discussion would be an absurd concept for a monkey population. Prosthesis seems to me the most likely source of change in the foreseeable future.

Huxley: Haldane also raised the very good point, that we need a new terminology before we can begin coping at all adequately with the subject.

Lederberg: I would like to stress that these are *not* long-term problems, they are upon us now, and we cannot afford to wait indefinitely for the kind of philosophy on which we can base our solutions.

Comfort: We have all been assuming that the exponential progress of science can go on indefinitely. I would have thought from what we said earlier about rates of change in society that our descendants might well benefit from a period of relaxation. They might have a period in which they have a rather less intense social drive, and perhaps become more shallow and superficial in some of their attitudes, by our standards; at the same time they may have less incentive to go on adding to discovery at quite our rate. I wonder if the preoccupations we have shown here may not seem as grotesque to our descendants as some of Oliver Cromwell's theological discussions do to us. We may be going to produce a generation, not so much of scientific puritans or of scientific activists, but of beatniks who are going to enjoy, for a while at any rate, the proceeds of what we are now laying down. Though Professor Haldane has not suggested it in quite this form, I feel he hinted at this when he talked about some of the uses which we may make of increased somaesthesia. The ancient Indians cultivated the art of love for both religious and practical reasons, and I think we may find ourselves cultivating similar aesthetic elaborations of pleasure. At least I hope our descendants will do so.

Huxley: I am sure you are right, Comfort, in thinking that the exponential curve of the growth of science will start bending

over in the not very distant future, and become asymptotic to some sort of limit; just as the growth of cities is already curving over and reaching a limit beyond which they cannot function. Similarly if we have too many scientific discoveries in a given time we may not be able to assimilate them.

Crick: One has to distinguish between knowledge reaching a limit and the *rate* of acquisition of knowledge reaching a limit. It is reasonable that the rate should be self-limiting, but unfortunately it is likely to reach saturation at a very high level. Moreover, I think that while there are competing societies this problem will remain. After all, one of the reasons why we get such support for science is because it has economic and political value to individual nations or groups of nations: this is why much of the money is made available.

Perhaps we shall have to have a world in which we are put back artificially into a series of small communities which compete *culturally* in some way. There are also certain real problems in connexion with world government, and with the limitation of population. How are nations or social groups going to agree to limit their populations when one wants to grow bigger than another, or fears to grow smaller?

The development of biology is going to destroy to some extent, our traditional grounds for ethical beliefs, and it is not easy to see what to put in their place.

Price: I would like to draw some further consequences from the exponential growth of science[1]. One of the reasons why we are getting so much money and support for science is precisely because, in the well-developed countries, we are becoming more and more nervous simply because the curve *is* bending over. Deceleration is already setting in and we have nearly attained a saturation state. What is very odd is that the later a country "takes off" into that industrial revolution, which is now ending in some older countries, the faster technological progress goes. The old scientific countries of Europe plus America are now very rapidly reaching the point where they will be producing less than fifty per cent of all scientific discoveries. Our questions should be posed not in terms of what

we are going to do with science, but what *they* will do. Very rapidly, within the next generation, the present "western scientific world" is going to become a minority, since the under-developed countries grow so very quickly. Add this to the nervousness of an over-developed country with a saturated rate of scientific advance, and the consequence to be expected is, not a moratorium on the growth of science in which we can pay some attention to other aspects of life, but a deep reaction in quite the opposite direction, towards competition and the maintenance of technological supremacy. I regard this as a very dangerous situation.

MacKay: In this context a serious limit may be set by the problem of information retrieval. As Norbert Wiener pointed out some years ago, the more information you produce, the more competent a man must be before he can sort out what is worth reading, and the more of his time he has to consume when he might have been doing productive work. No matter how hard we mechanize, this is liable to lead to some kind of levelling-off of progress to which no answer seems to be in sight.

Crick: The total *rate* of cumulation of scientific knowledge is liable to be maintained, regardless of whether the process is efficient or not.

Price: But science is not at all happy with a constant rate; science is an exponential animal and it gets terribly unhappy if you deny it the right amount of exponential growth.

Comfort: It isn't science, but the *scientists* who are unhappy, and I think that if we were like the Samoans we should be less violently motivated to maintain this frantic "progress".

Price: I am not sure that it is a social property of the scientist; it may well be a property of the interconnectivity of the network of knowledge.

Huxley: Surely science may evolve and curve over towards fewer but better-integrated networks of study. This will change the whole problem of publication; there will be fewer little separate bits of science that need to be added up; scientists will be working on large co-operative projects, which will be co-ordinated.

Price: Yes, we are changing the whole system of scientific communication; it is now clear that the scientific paper is a dead duck. One just doesn't lay down knowledge in little bricks like this any more. We have relinquished this sort of task to machine-handling and the scientist now does something rather different. He no longer has a personal stake in immortality by becoming Mr. Boyle of Boyle's Law: a quite different sociology of knowledge is coming into being.

Brain: It is obvious, I think, that we cannot isolate extrapolation from values. What is going to happen depends on what people will think good, and what we would like to happen depends upon what we now think good in these various contexts.

I want now to ask you whether in fact there is any conclusion to our discussion; whether you think that anything ought to be done about it, and if so what? It seems clear that part of the difficulty of the situation in which we find ourselves comes from the fact that science operates very largely without foresight. People do good, in fact, that evil may come, though that is not their intention. It is a good thing to abolish malaria, but the net result is that the population increases, which puts a strain on the current food supplies. It was a Nigerian economist writing about this who said: "I know I ought not to say this, but I do hope that before they improve hygiene any more they will do something to improve agriculture." Chisholm made the point that people in under-developed countries are no longer accepting the situation as they used to—a situation in which 50 per cent of the children never grow up, for example, a situation only made tolerable by ideas such as reincarnation, a situation which rather recalls the acceptance by our great-grandparents of the loss of several children in every family, which was taken almost as a matter of course. Contact with European culture is rapidly changing all that.

Then we come to the time factor. As Brock has said, we may now foresee to some extent what ought to be done, but can we catch up with events? Because what is happening now is the product of what was done over the last twenty-five or thirty years. It seems to me that questions about the world's food

supply, or the proportion of people who are undernourished, are almost meaningless; because when you actually come to do anything about it, however much you may achieve at the top level, you have ultimately got to come down to some village in Nigeria, which is on a track miles from the main road, which is bound by local cultural traditions, by agricultural techniques, by lack of seed potatoes. It looks as though ultimately whatever we may do at the top we come down to doing good by minute particulars, just as we have to change people's minds, if we can change them at all, individually.

We seem to be agreed that one essential is to educate people more in biological facts as a necessary preliminary to any action. Although we have heard so much about conflicting values, I have not felt that they are really the obstacle they seemed to be to start with; because I think we have seen that we do not deal with an abstract value and particular facts, but with a feedback mechanism in which both get changed. So, when we come to look back at views on population and birth control, we see a reflection of what is actually happening now. In time the force of facts alters the effect of values and action is finally taken.

Then there is the question of the price of progress, and the point that Koprowski raised about the effects of antibiotics in ridding us of infection. It is certainly true that as a result of immunization against poliomyelitis, virus infections are now seen which were not at all common before, leaving the clinical picture very much the same as it was. I am sufficiently optimistic to think that many of these problems will in fact be overcome. Part of the price of progress obviously is that people who would have died earlier, live on to provide geriatric problems; though I am sure they would rather live on to get rheumatism or strokes in old age than die at thirty-five of pneumonia.

There are also the iatrogenic diseases, where new drugs produce fresh diseases or monstrosities. Here there is a curious disturbance of the sense of proportion. When we had one or two cases of smallpox introduced into Britain there was something like a panic, with people queueing up to be vaccinated.

At the same time, they tolerate twenty thousand people a year dying of lung cancer, five or six thousand dying in car accidents, a hundred thousand or more injured in road accidents, with apparent equanimity. Perhaps it just depends how many people are killed at a time. A hundred in an air crash gets much more reaction than a hundred people separately on the roads.

I would like to turn to the point that Haldane made about the problem of controlling degenerative diseases which occur in later life, presumably based on genetic changes but not selective because they do not manifest themselves until after the reproductive period. It would obviously be difficult to eliminate those, I imagine; but we may hope to do something in the way of prevention and treatment. But here again there is a problem, because one suspects that the causes of atheroma possibly, cancer possibly, may lie many years back. A biochemist in Ibadan made a speculative suggestion to explain why atheroma is so rare in Nigerians: it may be that deficiency of diet in childhood is the factor which prevents the preliminary changes which, many years afterwards, lead to the development of atheroma. If that is the sort of thing we have to look at, then the problem of preventing these diseases is going to be very long-term indeed, even assuming you could persuade people to do the thing which is going to prevent them from becoming ill years hence: which Haldane suggested might require compulsion.

However that may be, there is perhaps a philosophical or religious aspect to what Koprowski said; obviously we have to live with imperfection, however effectively we may improve people by scientific methods. We are left with this residue of imperfection to which we have to adapt ourselves and which, of course, has been one of the problems for religions through all the ages.

I suppose we could all agree, whatever our fundamental beliefs, that it is desirable to have some standard of values upon which action can be based, and it is equally desirable to get some sort of satisfactory emotional relationship to the nature of things

as a whole, even though it may be very partial and occur at a low level. Here I would like to ask a question: what is the implication of mental adaptation in the evolutionary sense? Men begin with erroneous scientific beliefs and erroneous religious beliefs, but how far are these different universes of discourse, how far are they different kinds of symbolization? We use symbols in science for certain purposes, and there are adequate methods of verification. What about the functions of other types of symbolization in life? The most obvious example is art, but are there other fields of discourse, other uses of symbols which do not conflict with science but supplement it, yet nevertheless are so different that we cannot translate the one into the other. If that is true, is there not scope for different sets of symbolic language, which are equally important in our relations with things as a whole? And if that is so, what is the part played by these systems in evolution? Is it a condition of man's survival in the long run that he shall not adopt delusory ideas, either scientific or otherwise, but that he shall have some adequate form of symbolization which adjusts him to things in general and is associated with emotional satisfaction?

Finally, I would like to mention the point which Szent-Györgyi raised, namely, that we have reached the stage where we cannot understand the things we discover. I have the impression from what he said that it was rather that we cannot picture what we have discovered, but that we have other methods of understanding it. But does that apply elsewhere, does that apply in the sphere of ethics and action? Have we reached the stage now, at which man has evolved so that he can no longer control the things on which his future destiny depends?

Bronowski: I resisted the temptation to reply earlier when Colin Clark made what I thought was an excessively provocative statement about values. But since Lord Brain has raised the issue again, and related it so forcibly to our future conduct, I would like to make a statement about values as I think humanists see them, or at any rate as my kind of humanist sees them. I think it will be found that these human values can

have a profound influence in shaping the future towards ends which people can regard highly.

We have seen over the past three hundred years a scientific revolution whose effect on public opinion, and on the public tolerance of acknowledged evils—evils acknowledged by Christians and non-Christians alike—has been phenomenal. Slavery, cruelty to animals, public execution, a thousand evils have been abolished by a public opinion which has been moulded by science. These were evils which those who sat on the Inquisition recognized as evils, but did nothing to put right because they were too busy doing what they thought were more spiritual things. It is therefore, in my opinion, quite wrong to say that the accumulation of factual evidence in science has had no ethical effect. The very facts about how Jews are related to non-Jews, and Negroes to non-Negroes, has made civilized men feel differently, and feel ashamed, on these issues. I therefore deny those classical letters to *The Times* which bishops and retired admirals write every so often, that start with the phrase "Science is neutral". Even as an accumulation of facts, science is not neutral, because it invades the conscience of people with a sense of right and wrong applied to Minute Particulars—if I may borrow the phrase which Lord Brain has so eloquently borrowed from William Blake.

This is much, but there is much more. The deeper effect of science over the past three hundred years has been, not in the accumulation of true facts, but in making people aware that the very search for what is factually true is itself an ethical activity. What is true in a factual sense is quite differently regarded today from the way it was regarded three hundred years ago. A man who wants to find out the truth, even about how I am going to vote at the next election, is now more highly regarded than he was three hundred years ago—not to mention the time of the Inquisition.

The great ethical force of science has proved to be the dissemination of the idea that truth is a thing which will in some way help us all. In this, we don't have to claim that truth is good, or beautiful, or absolute. We simply recognize that men

have found that it is easier to run a society made up of independent individuals if they all acknowledge what is true.

Man is an extraodinary creature, and he has one gift to which we have made no reference at all: he is the only social solitary. He is the only creature who does his best thinking and working alone, but does it only in the setting of a society. This conflict, or this interplay, between what is socially acceptable to his society, and what is personally desirable to him, makes up the whole problem of ethics. We have now learned to acknowledge that to be truthful makes it easier for man to be both solitarily creative and socially sustained than any alternative behaviour. I regard that as the major step that science has made in producing an ethic.

Now as soon as you acknowledge the effective importance of truth, you bring in its train a whole system of values. You have to have justice, you have to have independence, you have to have freedom. Since I said all this in detail in a book, *Science and Human Values*, I won't elaborate it here[2]. There I showed that once you organize a set of people like the Royal Society, or the Academy of Sciences, so that they have an overriding allegiance to what is factually true, then you build up, of necessity, social values between them. If cheating is not allowed, however expedient the occasion, then people like Kammerer prefer to shoot themselves rather than live in shame in the society of scientists.

The Old Testament and Puritan virtues of justice, tolerance, freedom, independence—these are the virtues that have been spread by what I call "the scientific ethic". However, the scientific ethic is not the whole of ethics. The Old Testament does not contain all the virtues; and if I for one regard the growth of the biological sciences as critical for the future of man, it is because they may make accessible those inner truths, the psychological truths, which so far have not been fostered by science. So far, these personal values—the new Testament virtues of love and tenderness, for example—are enshrined in works of art: in *Anna Karenina*, the *Dialogues* of Socrates, and the paintings of Rembrandt. I do not know how they are communicated. Yet the arts do somehow give us the feeling of sharing

with other people a common psychological truth. This is the universal importance of works of art. The virtues of kindness and love and altruism are communicated by them, by the recognition that what is psychologically true for me is in some sense also psychologically true for you.

I think that the continuing development of science, and particularly of the life sciences, will make a unity of the values of science and of our artistic values. It will do so by disseminating and illuminating the feeling that human beings do share other experiences than those which can be published in scientific papers. I am, therefore, not in the least ashamed to be told by somebody else that my values, because they are grounded in my science, are relative, and his are given by God. My values, in my opinion, come from as objective and definitive a source as any god, namely the nature of the human being. And they differ from those of people who claim that their values come from God in only one respect; that the human being is still developing, and therefore my values are expanding and changing and are not written down on tablets of stone. That makes my values richer, I think; and it makes them no less objective, no less real, than any values that can be read in the Testaments.

MacKay: With all due respect, Bronowski has got the cart before the horse. What he has said shows in fact that it was the concern for truth and the like which begot science, not science which begot the concern for truth. Such ethical values are, of course, essential to the practice of science, and the more people we teach to be scientists the more we should disseminate these values. As a matter of historical fact, however, it was mainly Christian men, inspired by a more biblical attitude to nature than the Aristotelian-scholastic tradition had shown, who founded the Royal Society.

What science (as such) does for us has something of the double-edged neutrality of a searchlight. Science can spotlight features we would not otherwise have known in the jungle of our existence. This makes us responsible both for choosing where to point its light, and for making judgments of value in the situation it reveals or clarifies.

Where, however, are we to find a basis for these judgments? Crick's honest admission that science does not provide us with such an ultimate basis accords with my own feeling. If we let go of our anchor in the one dimension which has some hope of answering questions of value—namely the religious dimension, in which the question of the origin and meaning of existence is asked—then we are indeed ethically anchorless. When you look closely into the logic of the arguments people have advanced for throwing away the rope, you find it, I believe, as full of *non sequiturs* as any produced by their opponents. The experience of this has helped me, like many others, to a strong conviction that for our generation the way forward will be first to look back again, and to recover what we have irrationally lost in the enthusiasm of opposing people who drew mistaken inferences in the name of the Christian religion.

To go on to a more technical point, it seems to me that our biggest lack at the moment is in our whole understanding of the nature of the process of valuation. For an acute analysis of this problem I would particularly like to recommend the chapter by Sir Geoffrey Vickers in a forthcoming symposium entitled *The Environment of the Metropolis*[3].

Our understanding of what it is to arrive at a common judgment of value is as primitive by comparison with what we would like it to be, as pre-scientific thought is by contrast with science today. One of our most pressing needs, I would suggest, is for men of a greater variety of experience than scientists to get together with us and try to understand more about the nature of the characteristically human process by which valuation is performed.

Huxley: One of man's major properties is that he is always evaluating and creating values. How has this function of valuing developed and how and why have his values evolved in his relatively brief psychosocial existence?

Young: You refer only to man in his evolution as a psycho-social creature, but I think too little has been said about the early stages of biological evolution. We have talked only about the past ten thousand years as a guide to the next ten thousand

years, but there is surely something to be learned from the previous five hundred million or so. There seems to be some principle of change inherent in the system which we do not yet understand, and which I feel sure has great lessons for us.

Huxley: I agree that the roots of human valuation are in our animal ancestry, and we have always to relate our thoughts on ethical and other values to the studies of the ethologists, who are doing remarkable pioneer work on behaviour.

Comfort: I would like to take up what Bronowski said. Not only has science given us a completely new valuation of integrity, but it seems to me the important difference from past hypotheses is that science makes it to some extent self-validating. If you are going to adopt the attitude that for ideological reasons you will have none of Mendelian genetics, or you will have none of Einsteinian physics, then as a consequence you will not have beef or you will not have radio sets, in proportion to the degree that your opinions are irrational. Surely, the fundamental difference from past attempts to value reality in philosophical or religious terms is that now you are subject to this crude empirical test of performance. It gives me the hope that in future we shall have less irrationality merely on the grounds that irrationality does not in fact work.

Hoagland: Anatol Rapoport has pointed out that while science has its own myths, as do all systems of thought, science can survive the smashing of its myths repeatedly and indeed gains strength from this very process. Hypotheses are destroyed by experiments and new ones are built up and confirmed or overthrown. Moreover, the people who destroy the myths of science are respected and even given Nobel prizes. They are not persecuted as heretics as they are under authoritarian systems of thought.

Szent-Györgyi: I think Lord Brain's remark about planning in science is a most important point, because progress can be harmful if it is not planned. For instance, we have introduced death control without birth control, and even feeding the hungry can turn out to be wrong. I fed the chickadees in my garden last year because they were hungry and now I have

ten times as many chickadees as I had last year, and again they are hungry, only there are ten times as many of them.

Chisholm said that we all act in two qualities, as individuals and as members of a group. I would go further and emphasize that we have two sets of reflexes, and the evaluation reflexes are entirely different in the individual as compared with the group. Let us consider the following list:

Murder,
Robbery,
Rape,
Destruction,
Lies.

These are the most common crimes in decreasing order of gravity. But they are crimes only as long as they are committed individually within the group. When they are committed by our group in its struggle with other groups, they become virtues, the road to glory. The rape of the Sabine women is still one of the golden chapters of Roman history!

Bronowski: They were only solving a population problem!

Szent-Györgyi: One of the great troubles of our time is that governments represent group morality. I can even feel it within myself when I am going to the polls, and become for a while a small part of the government; then my values become those of the group and not of the individual. In Massachusetts at the last election we elected to high office somebody who was actually in jail for fraud; apparently we trusted him to represent our group morality better than any Harvard egg-head.

Lederberg: Whatever the value of this ethical discussion, we can hardly take it on ourselves to decide these issues for the rest of the world. I do believe, however, that it is extremely important that the rest of the world should have the opportunity to discuss them; and as Crick has pointed out, public information on the possibilities of human modification, which is part of what we are talking about here, is not widely available or prevalent, particularly in the seats of high political power.

The biological competence of governments has been called into question, and perhaps we should spend some time thinking

what to do about that. This is a practical issue of tremendous importance if this kind of discussion is to reach all the levels where it ought to be noticed. It is the technical judgment of time-scale of these considerations which is most important.

Huxley: What we want is neither a very long-term nor a very short-term plan; but special attention should be paid to better education, which would involve only a one-generation lag.

Comfort: I think it would be a great mistake for us to brief the Cabinet on these lines. I feel sure we could only put ideas into their heads! What we want to do is to brief the public before the Cabinet finds out more about science than it now knows, to enable the public to control the delinquent activities of the government in the future.

Bronowski: Szent-Györgyi implies by his list of private crimes and public virtues that our great need is to stop people who have had a classical education from reaching positions of power—I draw this conclusion because, of course, the group virtues that the list represents are the values taught by a classical education!

Szent-Györgyi: Individual and group behaviour show a complete reversal. As members of our group we not only *take* life easily, we even *give up* life easily. All our individual reflexes serve to preserve our lives, but most of us are ready to die for our country. As individuals we try to enrich ourselves, but for our group we readily give up our belongings. We have two different, if not completely antagonistic, codes of behaviour. So when discussing evaluation we should always state which code we are using.

Wright: Would you carry this principle right through, so that personal *virtues* would become, so to speak, public *vices*?

Szent-Györgyi: Yes, indeed. Refusal to kill, for instance, is one of the gravest offences in war.

Koprowski: I wonder what right we have to assume, as a group, an attitude of superiority over our governments. If we are to be governed by somebody I am not sure that we should

choose *this* group, for instance, as an ideal government for any country.

Comfort: If we were in the government's shoes, we should be just as much of a menace to everybody else, in spite of our superior knowledge. The error lies in allowing any group in society to arrogate to themselves the power which governments arrogate to themselves, and which perhaps Muller appeared to arrogate to scientists in his paper, perhaps through overconfidence. I am not attributing improper motives to governments. I am merely saying that they have an impossible task, and one which we should encourage them to lay down.

Hoagland: I cannot altogether agree with Szent-Györgyi on some of these matters. When one compares the views of responsible people in government with those of most intellectuals one finds much more in common than is apparent superficially. The stereotypes of military people I have found may not be at all characteristic of top-flight people in government and in the military establishment. They are well informed and deeply concerned about these issues. They may be even more frustrated than we are, because tackling these problems at a practical level is a daily issue with them.

In the United States today there are a number of groups that are much concerned with ethical issues; for example, there is a group called the Institute for Religion in an Age of Science. It consists primarily of scientists, philosophers and theologians, who get together to discuss some of these matters. There is also a new Institute on Ethics being developed in New York which plans to send western representatives to India and other countries, to meet scholars and discuss problems of common human concern. It is surprising, when one meets such people, to discover the extensive common ground that is true for all of us. The humanitarian viewpoint, regardless of one's formal religion or its lack, seems to permeate increasingly into such international discussions.

There is a deep feeling of alarm and frustration, at all levels of society in the United States, in relation to nuclear war. I have had occasion to give a number of talks to lay groups,

including some very conservative groups of business men who a few years ago would have been hostile to the views I have expressed about world government under law, disarmament and arms control and the curtailment of national sovereignties, including our own. There is much more receptivity for such views today.

Price: The point surely, is not that individuals in charge of the group have ethics opposed to those of normal individuals, but that the group as a whole has some sort of homoeostasis that is opposite in sign to that of the individual. Perhaps it is worth pointing out that scientists are very peculiar in their organization. They are the one group in which the ethics of the whole appear to be the same as those of the individual. I gather that quite a lot of discussion has been directed towards this type of scientific understanding, which might give one a group ethic similar to that of the individual, a point that is not shared by the unscientific political control of the group.

Chisholm: I want to return for a moment to Szent-Györgyi's list. We have a system of ethics for individuals to which, generally speaking, we all subscribe, within our own culture at least; but we don't expect our governments, that is to say our group, to subscribe to the same set of ethics at all. The group inherits its own definition of its own ethics in relation to its national purpose, which has been inherited all the way back from the old man who made the law by his own whim or will. The nation inherits that same freedom from external control, so that we still do not expect our governments to be civilized, that is to say, we have not set up a law to which our governments are expected to conform. I think the mark of civilization is essentially a law that is mutually agreed and demands conformity. We have left our nations out of it because this was the limit of our feeling of integration, the limit of our area of responsibility up till now. But the next step in social evolution and indeed moral evolution, it seems to me, is to require governments also to become civilized. This is what I think Szent-Györgyi is saying; we are civilized up to our national boundaries but beyond that we are not.

Trowell: Speaking for the religious approach, I can find little basis for disagreement with much of Bronowski's humanist point of view. There are, of course, some other things we should like to add for those who voluntarily choose to be associated with us in Christian religious belief, things like worship and the sacraments, which to us are a source of strength and guidance. But when we talk about these basic ethical considerations which concern all humanity, I feel we are essentially in agreement. We may all have misgivings because we don't know enough about the genetical basis for planning; also there are many other aspects, psychological, social and religious, which we have barely considered. Speaking for my own, the Anglican Church, I think we feel that religious ethics must evolve, even progress, although we look to certain great sources for help in this matter, religious sources such as the Scriptures and the tradition of the whole Christian Church.

MacKay: Dr. Trowell would scarcely have made that remark had this been a group of German biologists of the Nazi variety. Certainly Christianity is itself a humanitarian and humanist view of the world. It does indeed say more than those who are humanists but not Christians, but in so far as it is a humanist view of the world, there is a great area of overlap with others who call themselves humanists. To that extent, of course, one should expect collaboration and co-operation to be possible and vital. But the important thing is to be prepared for genuinely creative clashes in fearless honesty when issues arise on which neither the Christian nor the humanist "handbooks" have a clearly worked-out answer. One such issue was slavery, which Bronowski mentioned. And in view of his remarks it is only fair to point out that it was Wilberforce, one of the enthusiastic Evangelicals of the Clapham sect—Wilberforce the Christian, not the scientist—who was the moving spirit in the abolition of slavery. Here, as it happened, their Christian religion brought them to see a need for humanitarian reform that none of the scientists or theologians of previous generations had urged with any force.

But surely it is pointless, as well as irrational, to seek credit

for science as if it were in competition with religion in these matters. Whatever the merits of particular religions, they are logically no more rivals of science than a compass is of a map. From a Christian standpoint at any rate, I believe that God expects a man to do equal justice to scientific and to religious knowledge, since He is the giver of both.

Crick: The considerable degree of agreement which certainly can be reached between "biological humanists" and people with a Christian background appears to me to be an historical accident. When one first discards Christian belief, more of the ethics and the patterns of thought remain than one could possibly anticipate until over the years one has thought about a large number of issues like these we have been discussing. I foresee that if we were to remove the Christian ethic completely (or those of any other religious system) and simply go on roughly, by a rule of thumb, with our biological knowledge, we might well come to a quite different set of ethical values. But I do not see how these can be given a *logical* justification. I do not think they will be the same as the present ones for the reason that MacKay gave, namely, that all the time new facts and values are being fed into the system; society can in fact develop in different ways and may thus end up with different stable systems of thought. It is perfectly true, as Bronowski says, that in order to pursue science you have to have certain values concerning truth and so forth, but they do not necessarily coincide sufficiently with the Christian values for other practical purposes. Take the suggestion of making a child whose head is twice as big as normal. There is going to be no agreement between Christians and any humanists who lack their particular prejudice about the sanctity of the individual, and who simply want to try it scientifically. One must face the fact that there is eventually bound to be a conflict of values. It is hopeful that at the moment we can get a measure of agreement, but I think that in time the facts of science are going to make us become less Christian.

Haldane: We have left out what may be the most important ethical fact about applied science, namely, that it magnifies

pre-existing evils until they are seen to be intolerable. Two hundred years ago, you and I might have been walking about with swords, but we are not now allowed to walk about with Mills bombs or automatic pistols. I pointed this out forty years ago, and was rather complacent about it. The trouble is that everything is happening too quickly with these atomic bombs. When an evil is sufficiently magnified everyone recognizes it as an evil, and that is one of the things that science does.

Wright: To return to the question of what we, as a group, can do about this: I have worked with politicians a great deal and I deprecate the view that they are a different race. I think government has been defined as the art of the possible, and this in fact is what the politician is trying to do. As a scientific adviser it was *my* job to point out to the politician what I felt to be desirable, after obtaining as much information as I could on a given scientific point. But it was *his* job to see what he could get done. This is less easy, because he has to measure the possibilities of public acceptance of alternative policies. It seems to me that we overlook this aspect of what *can* be done, and that we should not say "Well, we as scientists would do this, but of course the politicians stop us." This is a negative approach; we and the politicians must together try to discover how we can take the people with us. This is primarily, of course, a matter of education.

Price: I would like to take up Wright's challenge. There is something we can do directly or very shortly in the future. Part of the business of the transition to a Big Science phase is that scientists are becoming very much more numerous and are becoming immensely more powerful and prestigeous. Within this generation the scientist will cease to be the man on tap, and become the man on top. The motivation of scientists seems to be changing in an interesting manner, so that the course of direct political action, previously anathema, now seems to be becoming respectable. Scientists are now extruded rather more rapidly and numerously from the research front and they get—in the vernacular—kicked upstairs to positions of political responsibility, so that many scientists actually have

their hands on the controls of political action. This is happening within the present generation and is one of the most optimistic things about the future of man.

Wright: I agree, provided it is not simply pure "scientists" to whom you refer, but people who have had a broad scientific training or background.

Medawar: Groups of this kind usually end up by agreeing on one thing, namely, that more education is what is wanted. I am unable to see how that view can be reconciled with the incredible diversity of opinion which has been expressed here. I really do not know, even if we took a census of opinion, what principles we would teach or what beliefs we would try to inculcate. This is the thing that has impressed me most about this meeting—the sheer diversity of our opinions, not merely between people like Trowell and Crick, but between people in the same narrow profession. I think this diversity of opinion is both the cause and the justification of our being obliged to do good in minute particulars. It is the justification of what Karl Popper called "piecemeal social engineering". One thing we might agree upon is that all heroic solutions of social problems are thoroughly undesirable and that we should proceed in society as we do in science. In science we do not leap from hilltop to hilltop, from triumph to triumph, or from discovery to discovery; we proceed by a process of *exploration* from which we sometimes learn to do better, and this is what we ought to do in social affairs.

Huxley: Much advance, both in biological evolution and in psychosocial evolution, including advance in science, is of course obtained by adding minute particulars, but at intervals something like crystallization from a super-saturated solution occurs, as when science arrives at an entirely new concept, which then unifies an enormous amount of factual data and ideas, as with Newton or Darwin. Major advance occurs in a series of large steps, from one form of organization to another.

In our psychosocial evolution I believe we now are in a position to make a new major advance, for instance in education. We can now educate people in the evolutionary concept

and in the ecological concept, neither of which were in existence a hundred years ago (except in a very rudimentary form) but which are now turning out to be very important ways of organizing our thinking about life and its environment. Indeed there are many important new concepts which we could bring out in a radically reorganized educational system.

Brain: We might end our symposium with another remark of Blake's: "Without contraries is no progression." All that remains is to thank you all for coming, and to repeat what Bronowski so aptly said, "We met as colleagues and we part as friends."

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Publications include: *Regional Planning and Development;* "Recreational Land Use" in *Man's Role in Changing the Face of the Earth;* "Designing on New Land" in *Space for Living.*

J. B. S. Haldane
Genetics and Biometry Laboratory, Government of Orissa, Orissa, since 1962.

Reader in Biochemistry, University of Cambridge, 1922–32; Fullerian Professor of Physiology, Royal Institution, 1930–32; Prof. of Genetics, London University, 1933–37; Prof. of Biometry, London University, 1937–57; Research Prof., Indian Statistical Institute, 1957–61. Darwin Medal, Royal Society, 1953; Darwin-Wallace Medal, Linnaean Society, 1958; Kimber Medal, National Academy of Sciences, Washington, 1961; Feltrinelli Prize, Accademia dei Lincei, 1961.

Publications include: *Daedalus; Possible Worlds; The Inequality of Man; Enzymes; The Causes of Evolution; New Paths in Genetics; The Biochemistry of Genetics.*

H. Hoagland

Executive Director, Worcester Foundation for Experimental Biology, Shrewsbury, Mass., since 1944; and Professor of Biological Psychiatry, Boston University.

Parker Travelling Fellow from Harvard and Lecturer, Cambridge, 1930–31; Prof. of Physiology and Director, Physiological Labs., Clark, 1931–44; Guggenheim Fellow, 1944–45; President of the American Academy of Arts and Sciences.

Publications on sensory nerve impulses, electroencephalography, neuro-pharmacology, physiological time, adrenal stress physiology and biochemical aspects of schizophrenia.

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Biologist and writer.

Lecturer in Zoology, Balliol College, Oxford, 1910–12; Research Assoc., 1912–13, and Assistant Prof., 1913–16, The Rice Institute, Houston, Texas; Senior Demonstrator in Zoology, Oxford University, 1919–25; Prof. of Zoology, King's College, London, 1925–27, and Hon. Lecturer, 1927–35; Fullerian Prof. of Physiology in the Royal Institution, 1926–29; Secretary, Zoological Society of London, 1935–42; Romanes Lecturer, Oxford, 1943; Director-General, UNESCO, 1946–48; William Alanson White Lecturer, Washington, 1951; Alfred P. Sloan Lecturer, Sloan-Kettering Inst., N.Y., 1955; Visiting Prof., Chicago Univ., 1959; Adviser to UNESCO on Wild Life Conservation in Eastern Africa, 1960. Past President, Institute of Animal Behaviour; President, Eugenics Society. Darwin Medal, Royal Society, 1957; Darwin-Wallace Commemorative Medal, Linnaean Society, 1958.

Publications include: *The Uniqueness of Man; Evolution, The Modern Synthesis; Evolutionary Ethics; Man in the Modern World; Evolution in Action; The Story of Evolution.*

M. Klein

Professor, Director of Institut de Biologie Médicale, Faculté de Médecine, Strasbourg, since 1946.

Assistant, 1927, and Associate Professor, 1939, Institut d'Histologie, Strasbourg. Professor in Medical Biology, Faculté de Médecine, and Lecturer in Biology and Social Life, Institut d'Etudes Politiques, Université de Strasbourg.

Publications on experimental and clinical aspects of the physiology of reproduction and on the physiopathology of peripheral nerves.

H. Koprowski

Director, The Wistar Institute Philadelphia, Professor of Microbiology, Graduate School of Arts and Sciences; Professor of Research Medicine, University of Pennsylvania, since 1957.

Research Assistant, Department of Experimental Pathology, University of Warsaw, 1937–39; Staff, Yellow Fever Research Service, Rio de Janeiro, 1941–44; Staff and Assistant Director, Viral and Rickettsial Research Division, Lederle Laboratories, Pearl River, N.Y., 1944–57. President, New York Academy of Sciences, 1959. Alvarenga Prize of College of Physicians of Philadelphia, 1959. Consultant: World Health Organization.

Publications on virus infections, cancer, immune reactions and cellular transformations.

J. Lederberg

Professor of Genetics and Biology, School of Medicine, Stanford University, Palo Alto, since 1959.

Assistant Prof. of Genetics, University of Wisconsin, 1947–50; Assoc. Prof., 1950–54, Prof., 1954. Organized Department of Medical Genetics, 1957, Chairman, 1957–58. Visiting Prof. of Bacteriology, University of California, Berkeley, 1950; Fulbright Visiting Prof. of Bacteriology, Melbourne University, 1957. Organized Department of Genetics, Stanford University Medical School and was appointed Professor and Executive Head, 1959. Awarded Nobel Prize for Medicine, 1958.

Publications on microbial genetics, immunology and exobiology.

F. A. Lipmann

Member and Professor of Rockefeller Institute, New York, since 1957.

Research Assistant Kaiser Wilhelm Institute, Berlin and Heidelberg, 1927–31; Research Fellow, Rockefeller Institute for Medical Research, New York, 1931–32; Research Associate, Biological Institute of Carlsberg Foundation, Copenhagen, 1932–39; Research Associate, Department of Biochemistry, Cornell Medical School, New York, 1939–41; Head, Biochemical Research Laboratory, Massachusetts General Hospital, Boston, 1941–57; Associate, Harvard Medical School, 1946–49; Professor of Biological Chemistry, 1949–57. Member of National Academy of Sciences (Washington); Fellow Danish Royal Academy of Sciences; Foreign Member Royal Society (London) 1962.

Publications on metabolic energy conversions, discovery and identification of coenzyme A as group carrier in carboxylic acid metabolism, sulphate activation, and protein synthesis.

D. M. MacKay

First Granada Research Professor of Communication, University of Keele, Staffs., since 1960.

Radar research at Admiralty Signal Establishment, Witley, 1943–46; Lecturer, and latterly Reader, in Physics, King's College, London, 1946–60. Research into the limitations of high-speed electronic computers and into the foundations of Information Theory, 1946–50. Rockefeller Fellow in U.S.A., 1951. Since then, research has been chiefly into the information-processing organization of the brain, particularly in visual perception. At present building up an inter-disciplinary research group interested in the brain as a communication system, and the development of artificial mechanisms with "brain-like" function.

Publications on electronics, information theory, electroencephalography, experimental psychology, and "artificial intelligence".

P. B. Medawar

Director, National Institute for Medical Research, Mill Hill, London, since August, 1962.

Lecturer in Zoology, University of Oxford, 1944; Mason Prof. of Zoology, University of Birmingham, 1947–51; Jodrell Prof. of Zoology and Comparative Anatomy, University College, London, 1951–62; Croonian Lecturer, Royal Society, 1958; Reith Lecturer, 1959; Dunham Lecturer, Harvard Med. School, 1960; Former Member of Agricultural Research Council and University Grants Committee. Royal Medal of Royal Society, 1959; Nobel Prize for Medicine, 1960.

Publications include: *The Uniqueness of the Individual; The Future of Man.* Scientific papers on growth, ageing, immunity and cellular transformations.

H. J. Muller

Professor of Zoology, Indiana University, Bloomington, Indiana, since 1945, Distinguished Service Professor since 1953.

Assoc. Prof. and then Prof. of Zoology, University of Texas, 1920–36; Senior Geneticist, Institute of Genetics, Moscow, 1933–37; Research Assoc. and then Lecturer, Institute of Animal Genetics, Edinburgh University, 1937–40; Research Assoc. and then Visiting Prof., Amherst College, 1940–45. Awarded Nobel Prize in Physiology and Medicine for "discovery of the production of mutations by means of X-rays", 1946. Foreign Member, Royal Society, 1953.

Publications include: *The Mechanism of Mendelian Heredity* (with others); *Out of the Night: a Biologist's View of the Future; Genetics, Medicine and Man* (with others).

A. S. Parkes

Mary Marshall Professor of the Physiology of Reproduction, Physiological Laboratory, University of Cambridge, since 1961.

Hon. Lecturer, University College, London, 1929–31; member of staff, National Institute for Medical Research, London, 1932–61; Ingleby Lecturer, University of Birmingham, 1940; Addison Lecturer, Guy's Hospital, 1957; Chairman, Society for Endocrinology, 1946–51; Society for the Study of Fertility, 1950–52; President, Institute of Biology, 1959–61. Fellow of Christ's College, Cambridge; Fellow of University College, London.

Publications include: *The Internal Secretions of the Ovary;* and editor of, and contributor to *Marshall's Physiology of Reproduction*, 3rd edition.

G. Pincus

Research Director, Worcester Foundation for Experimental Biology, Shrewsbury, Mass., since 1956; Research Professor of Biology, Boston University Graduate School, since 1950.

Prof. of Experimental Zoology, Clark University, 1938–44; Director of Laboratories, Worcester Foundation, 1944–56; Research Professor of Physiology, Tufts Medical School, 1946–50. Albert D. Lasker Award in Planned Parenthood, 1960.

Publications include: *Recent Progress in Hormone Research* (ed.); *The Hormones* (edited with K. V. Thimann).

N. W. Pirie

Head of Biochemistry Department, Rothamsted Experimental Station, Harpenden, Herts., since 1947.

Demonstrator in Biochemical Laboratory, Cambridge, 1932–40; Virus Physiologist, Rothamsted Experimental Station, 1940–46.

Publications on biochemistry, especially on the separation and properties of macromolecules; articles on viruses, the origins of life, biochemical engineering, and the need for greatly extended research on food production and contraception.

D. J. de S. Price

Avalon Professor of the History of Science, Yale University, New Haven, Conn., since 1960.

Commonwealth Fellow, Math. Physics, Princeton, 1946–47; Lecturer, Applied Mathematics, Malaya, 1947–50; Consultant, History of Science, Smithsonian Institution, 1957; Donaldson Fellow, Institute of Advanced Study, 1958–59; Visiting Prof. of History of Science, Yale, 1959–60. Research in: Histories of scientific instruments; ancient astronomy and technology; modern physics; Middle English scientific manuscripts; quantitative measures on the growth of science; organization and administration of science.

Publications include: *The Equatorie of the Planetis; Heavenly Clockwork* (with J. Needham and Wang Ling); *Science since Babylon; Little Science, Big Science.*

A. Szent-Györgyi

Director of Research, Institute of Muscle Research, Marine Biological Laboratories, Woods Hole, Mass., since 1947.

Professor of Medical Chemistry, Szeged University, 1931–45; Prof. of Biochemistry, University of Budapest, 1945–47. Awarded Nobel Prize in Medicine, 1937.

Publications include: *On Oxidation, Fermentation, Vitamins, Health and Disease; Chemistry of Muscular Contraction; The Nature of Life; Bioenergetics; Introduction to a Submolecular Biology.*

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Ordained Priest in the Anglican Church and Perpetual Curate of Stratford-sub-Castle, since 1960.

Colonial Medical Services, 1929–58; Lecturer in Medicine and Paediatrics, Makerere College, University of East Africa, Uganda, 1935.

Publications include: *Kwashiorkor* (with J. N. P. Davies and R. F. A. Dean); *Diseases of Children in the Sub-Tropics and Tropics* (with D. B. Jelliffe); *Non-infective Disease in Africa.*

N. C. WRIGHT

Deputy Director-General, Food and Agriculture Organization of the United Nations, Rome, since 1959.

Commonwealth Fund Fellow, U.S.A., 1926–28 at Cornell University, N.Y., and U.S. Department of Agriculture, Washington; first Director Hannah Dairy Research Institute, Ayr, 1928–47; Hon. Lecturer, University of Glasgow, 1932–47; Chief Scientific Adviser (Food) to the Ministry of Agriculture, Fisheries and Food, 1947–59; Special Adviser to Imperial Council of Agricultural Research, India, 1936–37; Member Scientific Advisory Mission, Middle East Supply Centre, 1944–45; Special Adviser to Government of Ceylon, 1945; British Member of F.A.O. Mission to Greece, 1946; Chairman Food Standards Committee, 1947–59; National Food Survey Committee, 1948–59; F.A.O. Programme Committee (Rome), 1953–59; successively Chairman, Vice-Chairman and member of Committee for Colonial Agricultural Animal Health and Forestry Research, 1946–59; Secretary of the British Association for the Advancement of Science, 1963.

Publications include: *The Development of the Cattle and Dairy Industries of India; The Development of Cattle Breeding and Milk Production in Ceylon; Report of F.A.O. Mission to Greece* (co-author); "Economics, Supply and Distribution of Foods in the United Kingdom", in *Food Science;* "All Flesh is Grass", in *Research for Plenty*; "The Ecology of Domesticated Animals" in *Progress in the Physiology of Farm Animals.*

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Professor of Anatomy, University College, London, since 1945.

University Demonstrator in Zoology and Comparative Anatomy, Oxford, 1933–45; Fullerian Prof. of Physiology, Royal Institution, 1958–61.

Publications include: *The Life of Vertebrates; Doubt and Certainty in Science; The Life of Mammals.*

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* Index compiled by Mr. William Hill.

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